

A TEXTBOOK OF ORGANIC CHEMISTRY

Joseph Scudder Chamberlain





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A TEXTBOOK
OF
ORGANIC CHEMISTRY

BY
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PREFACE

The growth of chemical industries in this country during the last few years has created a new interest in the science and an increased demand for training in it. In no particular field is this more noticeable than in organic chemistry. The author trusts, therefore, that a new text may be acceptable, and that there may be found in it as much individuality as is possible in a book dealing almost wholly with well established facts and theories.

The student who is planning to fit himself for a life work in chemistry should take up the study of organic chemistry in the spirit of respect for the magnitude and complexity of the subject. He must go through the difficulties and not over or around them, but as he goes through them he must understand them as fully as possible, and the explanations in the textbook should be clear and adequate, though supplemented and emphasized by lectures and laboratory experiments. With these ideas in mind the author has endeavored to present the subject in a sufficiently elementary manner so as not to be beyond the grasp of the student in his first course in organic chemistry yet, at the same time, to make the book comprehensive in that it covers the entire field by taking up practically all of the important groups of compounds. Details as to properties and specific methods of preparation have not been emphasized in the case of individual compounds, except those of out-standing importance and interest. In the sense of being an abridged work, dealing with only relatively few and the simplest reactions and compounds, the book is not elementary. On the other hand the method of treatment in the free lecture style, with full and oftentimes repeated explanation of the steps involved in reactions and relationships, is elementary. To make the apparent complexity of organic chemistry clear and readily comprehended through definite and established relationships has been the chief aim.

The book is written primarily as a textbook for the undergraduate student and the instructor, but it is hoped that those who have

already studied the subject may find it of value for its general presentation. In its method and order of treatment the book is the expression of the author's experience during the last ten years in teaching the subject to students, most of whom have been planning to take up chemistry as a profession.

In attempting to correlate theoretical principles with industrial practice the author has not done more than to mention, in cases where it seems desirable, the fact that a given synthesis is the basis of industrial processes. No effort has been made, in most cases, to describe the technical procedure. In a few of the more common processes some description of the industrial procedure is given, but without any claim that it is exact in minute detail. It is important to emphasize the fact, that oftentimes in industrial practice, reactions while no doubt following the course worked out in the laboratory, are nevertheless frequently shortened by doubling up or by changing physical conditions, so that the process and the laboratory synthesis seem to be quite distinct. If this is kept in mind the author feels that the student will find no difficulty in gaining from a study of this text that fundamental knowledge of the theory of organic chemistry on which all practice rests, and at the same time a realization of the direct connection of this theory with the tremendous industrial application of organic chemistry to the life of the world.

A brief discussion of the separation, purification, identification, analysis and determination of molecular weight of organic compounds is given in an appendix instead of in an introductory chapter as is customary. In the presentation of the above topics, which belong more especially to a laboratory guide, only general methods are given without any of the details that must be observed in each case.

The author, in gathering material for the work, has had access to all of the standard books on the subject, and to a limited amount of original literature, and wishes to acknowledge herewith all such use of texts and journal articles. No references to literature have been made except where direct quotations have been used, as in the author's opinion, this would not increase the value of the book as a text for undergraduate students. A list of books used for reference will be found at the end of the volume, and to these in particular the author acknowledges his indebtedness.

In addition he wishes to acknowledge the assistance and coöperation of friends and associates who have read and criticized the manuscript, and of all others who have in any way assisted him in the large task which he has attempted.

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ORGANIC CHEMISTRY

PART I

A-CYCLIC COMPOUNDS—ALIPHATIC SERIES

INTRODUCTION

Organic and Inorganic Compounds.—The distinction between organic and inorganic compounds and the classification of all substances into these two groups, with the division of the science of Chemistry into the two fields of *Organic Chemistry* and *Inorganic Chemistry*, rests upon the fact that organic compounds were originally found in nature associated with, and as the result of, organized or living matter, *i.e.*, plants or animals. In this origin they were in distinct contrast to other known compounds which were termed *inorganic* because they were obtained from non-living matter, *i.e.*, the rocks, minerals and salts of the earth's crust. It was supposed that the vital process of living organisms was essential to the formation of the organic compounds, and as many of these seemed to be of an entirely different nature from that of the common inorganic compounds they were naturally believed to be of a distinct order and even unrelated to the ordinary chemical laws as worked out in connection with the study of inorganic substances.

In 1828 **Wöhler** made **urea** (p. 429) a product of animal life, from ammonium cyanate which is a substance that may be prepared in the laboratory from non-living or inorganic material. This epoch-making discovery, while in no sense so wonderful or so striking as many syntheses since accomplished, marked the beginning of the realization of the fact, that organic compounds, while produced in nature through the action of living organisms, were, nevertheless, of the same order and followed the same chemical laws as the compounds, which were non-living or inorganic. It soon became an established fact that many organic compounds could be made in the laboratory by reactions of the same nature as those used in making the inorganic.

Furthermore, as time went on, new organic compounds were made which had never been found associated with living things. Some of these were later found in nature while many have remained solely the product of laboratory reactions. Thus a large number of compounds became known as organic not because they were produced by living organisms but because they were directly related to other compounds originally so produced. The classification of compounds as organic or inorganic rests, therefore, upon *their relationship to other compounds* and not upon the circumstances of their natural occurrence. A compound is organic then because it is related to certain other compounds and it was found that those which were thus related and grouped together were all compounds of carbon or, to be more definite, were compounds of hydrogen and carbon or derivatives of these. The phrase, *hydrogen compounds of carbon and their derivatives*, becomes thus a truer description of what we now mean by organic compounds than their connection with organized or living matter.

All this does not mean that the vital property of organisms is simply a laboratory process or that having made a compound known to be produced in living plants or animals we have produced or can produce the living organism itself.

A. SIMPLER SATURATED COMPOUNDS

I. HYDROCARBONS OF THE METHANE SERIES.—PARAFFINS

GENERAL

The study of *Organic Chemistry* begins with the simplest compound of the two elements *carbon and hydrogen* and, as we proceed and the subject develops, we shall find that this and similar compounds are the mother substances from which all of the vast number of organic compounds may be derived. We can realize at once therefore the extreme importance of these fundamental compounds and also, the significance of the definition given in the Introduction that *organic chemistry is the chemistry of the hydrogen compounds of carbon and their derivatives*. The magnitude of the number of organic compounds will be realized when we state that according to the most recent enumeration in Richter's "*Lexikon der Kohlenstoffverbindungen*," 3rd. ed. and in the "*Register der Kohlenstoffverbindungen*," 1911-1914, there are more than 200,000 known compounds.

Hydrocarbons.—These hydrogen compounds of carbon are known as **hydrocarbons**, a name the significance of which is readily understood as indicating the two elements of which they are composed. It is well at the outset to guard against a confusion, which sometimes arises in the mind of the beginner, with another group of compounds having a similar name but which are of a distinctly different character, viz., **carbohydrates**. As the name indicates the carbohydrates were supposed to be compounds of carbon and water. Their true character will be understood later together with the reasons for supposing that they contained carbon and water. At present it is sufficient simply to guard against confusing **hydrocarbons**, *hydrogen-carbon compounds* and **carbohydrates**, *carbon-water compounds*.

Paraffins.—Carbon and hydrogen do not unite directly under ordinary laboratory conditions but in certain natural substances compounds of the two elements are present. Similar compounds of the two elements may also be formed by the decomposition of complex substances containing other elements than carbon and hydrogen. The hydrocarbons so found or formed are usually very stable compounds and

many of them show little affinity toward other substances especially the ordinary laboratory reagents such as alkalies, acids, oxidizing and reducing agents, etc. This statement applies especially to the group of hydrocarbons with which we begin our study and which, on account of their stability and inactivity toward other substances, have been given the name paraffins, from the two Latin words *parum*, too little and *affinis*, akin.

The common substance which we know as **paraffin** is composed of such hydrocarbon compounds.

Methane. CH_4

Marsh Gas.—The simplest hydrocarbon of this *paraffin series* and therefore the one with which our study will begin is known by the chemical name of **methane**, the series being also known as the *methane series*. It is found in nature and has a common name often used, viz., *marsh gas*. As this name indicates it occurs as a gaseous emanation arising from marshes where it has been formed by the slow decomposition of vegetable matter without the presence of oxygen or air. In winter air bubbles which form in the ice may sometimes be shown to contain methane and when opened give off a gas which will burn. This will be found to occur especially on ponds which contain large amounts of decaying vegetation.

Fire Damp.—Analogous to this non-oxidizing decomposition of vegetation in marshes and ponds is the slow geologic decomposition of plant life by which coal has been formed. Here also methane was produced and is now found shut up in pockets and crevices in the coal strata. The gas obtained from such pockets may consist of as much as 80 to 90 per cent methane, the remainder being mostly nitrogen. When the coal is mined this gas is liberated in the mine and there becomes mixed with air. When the methane gas and air become thus mixed in about the proportion of *one volume of methane to two volumes of oxygen (ten volumes of air)* there is produced an exceedingly explosive mixture which may become ignited by a spark or a free candle flame, and which in this manner is the cause of disastrous mine explosions. This explosive mixture of methane and air is called *fire damp*.

Coal Gas, Natural Gas, Petroleum.—From its natural formation and occurrence as marsh gas and as fire damp it is not surprising to find that methane occurs also as a constituent of three related sub-

stances, viz., *coal gas*, *natural gas* and *petroleum*. The two natural products, natural gas and petroleum, are in fact complex mixtures of hydrocarbons in whose formation various reactions have had to do. The discussion of the probable origin of these products and of their industrial importance will be considered at length later. Methane is also found as a constituent of intestinal gases where it is produced by the fermentation of carbohydrate food. After a meal of legumes the intestinal gases may contain as much as 56 per cent of methane.

Physical Properties.—Methane is a colorless and odorless gas. It is lighter than air and when pure may be readily liquefied. The weight of one liter of methane is 0.7146 g. and 22.4 litres (gram molecular volume) weigh 16.00 g. It is, therefore, 7.952 times as heavy as hydrogen which, as may be recalled, weighs 0.08987 g. per liter. The density of methane is then 7.952, and its molecular mass is 16.00.

Chemical Properties.—The chemical properties of methane are characteristic of this entire group of hydrocarbons, which on account of these properties are known by the general name of **paraffins**. Toward ordinary reagents such as sulphuric acid, nitric acid, chromic acid, alkalies and salts, methane is practically inactive. It burns in air or oxygen with a more or less luminous flame. By passing the products of combustion over calcium chloride and into lime water it may readily be shown that water and carbon dioxide have been formed, thus showing the presence in methane of the two elements hydrogen and carbon. If a cool surface is placed in the burning jet of methane gas a black deposit of carbon will be obtained. When mixed with oxygen in the proportion of *one volume of methane to two volumes of oxygen*, or with air in the proportion to yield this same ratio of methane and oxygen, *i.e.*, one volume of methane to ten volumes of air, an explosive mixture is formed, yielding, in case pure oxygen is used, only **carbon dioxide** and **water**.

Formula, CH₄.—The analysis of methane shows that it contains approximately 75 *per cent carbon* and 25 *per cent hydrogen*. This together with the facts in regard to its density and molecular weight give us the data for the calculation of the composition formula for the compound which has been established as CH₄, *i.e.*, one atom of carbon and four atoms of hydrogen. The reaction with oxygen may be written therefore as:



Synthesis from the Elements.—We may now consider methods for the formation of methane and in particular its synthesis from the elements. Though, as has been stated, hydrogen and carbon do not unite directly under ordinary laboratory conditions, they do unite directly when a mixture of the two elements is heated to 1200° , methane being the product.



Berthelot's Synthesis.—When carbon disulphide and hydrogen sulphide are passed together over heated copper or iron, methane is formed according to the following reaction:



This is known as **Berthelot's Synthesis**. As carbon disulphide may be made by heating together carbon and sulphur, and hydrogen sulphide is the product of the direct union of sulphur and hydrogen, we may consider this as an indirect synthesis of methane from the elements. A similar reaction occurs when carbon disulphide and steam are passed over heated copper.



Methane from Carbides.—Another method of preparation is of interest and importance because of its connection with theories as to the formation of methane and other hydrocarbons in petroleum. With some metals carbon forms compounds which are very stable at high temperatures, and which have been artificially produced in the electric furnace (about $3500^{\circ}\text{C}.$) by **Moissan**. These metallic carbon compounds, known as *carbides*, are, most of them, easily decomposed by water at ordinary temperatures, and when so decomposed they yield various members of the hydrocarbon group of compounds. A familiar example of this class of reactions is the one by which acetylene gas is made by the action of water on calcium carbide. The carbide of aluminium decomposes with water and yields methane according to the following reaction:



Laboratory Preparation of Methane.—As it is not practicable to obtain naturally occurring methane for study, we must resort to labora-

tory methods of preparation. Two general methods may be used for making it. The first is the synthesis from simpler compounds or from the elements as just mentioned and the second is by the decomposition of more complex substances. While the first method might be considered as the logical one with which to begin, it is not a practical one, and we, therefore, obtain methane by decomposing a more complex compound.

Methane from Sodium Acetate.—**Acetic acid**, as we shall understand before we have proceeded far in our study, is a compound related to methane. When the sodium salt of this acid, *i.e.*, **sodium acetate**, is heated it loses carbon dioxide, CO_2 , and methane is produced. In practice this heating is carried out in the presence of an alkali, *e.g.*, calcium or sodium hydroxide, which absorbs the carbon dioxide, and in this way assists in the reaction. In order that we may not be troubled by the presence of water, dry materials are used, the sodium acetate being fused to obtain it free of water. When this dry sodium acetate is heated with a mixture of sodium and calcium hydroxides, known as soda-lime, a gas is produced which may be collected over water. The gas so made is methane and is identical with that found naturally as marsh gas and as a constituent of fire damp, natural gas, coal gas and petroleum.

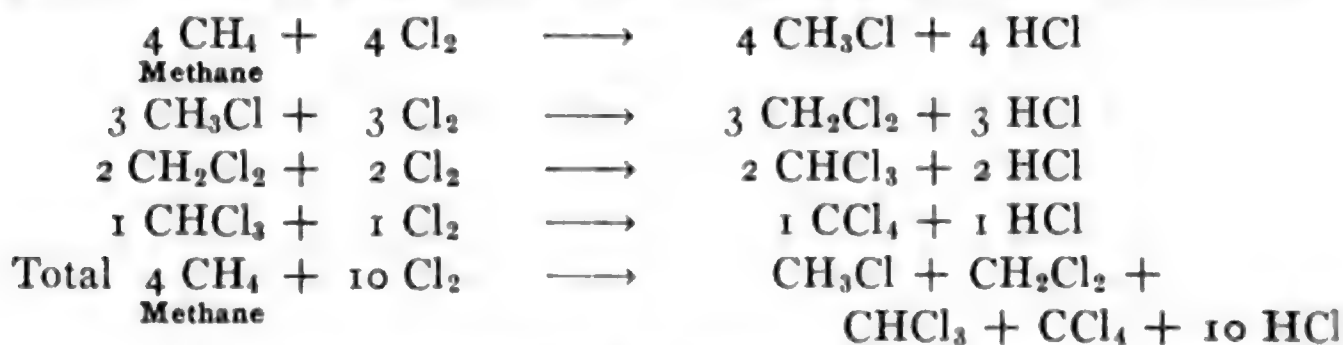
Reaction with Halogens.—We have referred to the inactivity of methane and the hydrocarbons in general. With only one group of substances does methane show any readiness to react. The members of the *halogen group* of elements, especially **chlorine**, react with methane in an exceedingly characteristic way, and it is by a study of these reactions that light is thrown upon the real nature of this compound, and the whole group of hydrocarbons that are similar to it, leading eventually to an understanding of the entire subject of organic chemistry.

When a mixture of **methane** gas and **chlorine** gas is ignited, or when an ignited jet of methane is burned in a jar of chlorine, action takes place and one of the products is *always hydrochloric acid* gas. When the action takes place suddenly as in the case of an explosion of a mixture of the two gases in the proportion of *one volume of methane to two volumes of chlorine*, the *only other product is carbon*. This reaction may be easily carried out in the laboratory and may be represented as follows:



The reaction is simply one of metathesis by which the chlorine unites with the hydrogen and leaves the carbon, and it shows us nothing more than did the combustion in oxygen, viz., that methane is a compound of carbon and hydrogen.

If, however, instead of by a sudden reaction the chlorine acts upon the methane *slowly*, as will be the case when a mixture of the two gases in the proportion of *four volumes of methane to ten volumes of chlorine* ($4\text{CH}_4: 10\text{Cl}_2$), is allowed to stand in diffused sunlight, the products of the reaction are wholly different. Instead of the chlorine taking all of the hydrogen and leaving only carbon it takes the hydrogen little by little. It is found, in fact, that *the hydrogen is removed, one atom at a time, and that as each hydrogen atom is taken by the chlorine to form hydrochloric acid an atom of chlorine enters the methane molecule in place of the hydrogen removed*. This reaction goes on step by step until all of the hydrogen is removed from the methane molecule and an equal number of chlorine atoms have combined with the methane carbon atom. Thus we may represent the steps in the reaction as follows:



When the reaction takes place as described the product is a mixture of hydrochloric acid gas and all four of these new compounds.

Chlor methanes.—What now are these four new compounds and how do they throw light upon the nature of methane? In the first place, all four of them have been isolated and their composition and formulas determined. They are called *chlor-methanes* and to distinguish them the *number of chlorine atoms in the molecule is indicated by a numerical prefix, i.e.,*

CH_3Cl , **Mono-chlor methane**

CH_2Cl_2 , **Di-chlor methane**

CHCl_3 , **Tri-chlor methane**

CCl_4 , **Tetra-chlor methane**

Two of these compounds are well known substances, viz., **tri-chlor methane**, which is the valuable anæsthetic **chloroform** and **tetra-**

chlor methane, which is known as **carbon tetra-chloride**, and is a solvent of fats, etc. These will be considered in detail later on.

Substitution.—A reaction of the kind we have just been considering in which *an element is removed from a compound and another element is put in its place* is known as a reaction of *substitution*, and the compound formed is called a *substitution product*. In the cases cited chlorine is substituted for hydrogen. The replaced element is always the hydrogen of a hydrocarbon or of the hydrocarbon portion of a complex compound, but the substituting element may be any monovalent element or a monovalent group of elements. A bivalent or trivalent element or group of elements may be similarly substituted for two or three hydrogen atoms at once. *The substitution products of any compound, therefore, are compounds derived from it by replacing one or more hydrogen atoms by an equivalent number of elements or groups of elements.* Among the most important substitution products are those in which hydrogen is substituted by (a) the *halogens* (*chlorine, bromine, iodine*), (b) the *hydroxyl group*, OH , (c) the *amino group*, NH_2 (the monovalent residue of ammonia, NH_3), (d) the *cyanogen group*, CN .

Theory of Substitution.—In these substitution products it has been shown that the substituting element or group not only takes the same place as the hydrogen which it has replaced, but in a certain respect acts like the hydrogen in the resulting compound, so that oftentimes the substitution products possess a similar character to the original compound. This may seem strange at the outset when we consider the difference in character between hydrogen and the examples of substituting groups we have mentioned, viz., *halogens, hydroxyl, cyanogen* and the *ammonia residue*. Objection on this ground was especially strong at the time the idea of substitution, particularly as applied to organic compounds, was first suggested by the French chemist, **Dumas**, in 1834. The theory was strongly opposed by **Berzelius**, who had previously advanced the electro-chemical theory according to which every element or group possessed definite electrical properties, some being positive and others negative. As hydrogen was positive and chlorine negative he held that it was impossible for one to take the place of the other in a compound. So many facts were brought forth, however, which confirmed the theory that it became generally accepted, and has been one of the most helpful of theories in connection with the development of our ideas as to the real nature of organic compounds.

We shall speak of this again and bring out some of the strongest facts which support the theory when we take up the chlorine substitution products of acetic acid.

Structure of Methane.—We shall now consider some additional facts in regard to these chlorine substitution products of methane, *i.e.*, the **chlor methanes**, and see how they help us to form an idea as to the structure of the methane molecule. By the *structure* or *constitution* of a compound we mean the *relation of each element or group of elements to every other element in the molecule*. In other words, the way the compound is built up or its structure. In its widest significance the structure of a compound, *i.e.*, the structure of its molecule, must have to do with the geometrical relations of the constituent elements or groups *in space*, and this will be our final consideration of the matter when we come later to treat of what is termed the *stereo-chemistry* of the molecule of organic compounds. For the present our consideration of the structure of organic compounds will have to do only with *the order in which the different elements or groups are joined together* to build up the molecule. Furthermore, it should be emphasized that our ideas of the structure of a compound are not simply notions as to how the elements may be joined together, but are *based upon definite known reactions*, and are but the *direct interpretation of these known reactions*.

Tetra-valence of Carbon.—At the beginning of our study of the real nature of the compounds of carbon we make an assumption which, though it is upheld by a majority of the facts, is still only an assumption. *In organic compounds the valence of carbon is four and is practically invariable.*¹ In inorganic chemistry, when an element unites with another element in more than one proportion, we explain it by saying that the valence of one of the elements has changed. For example, carbon forms two different oxides, one of which corresponds to the formula CO_2 , in which we say the valence of carbon is *four*. In the other the formula is CO , and we say the valence of carbon here is *two*. Now there is known a hydrocarbon which has only one-half as much hydrogen in proportion to the carbon as methane, its formula being C_2H_4 . In this compound, as we shall see later on, and in almost all similar cases in organic chemistry, the facts of composition are explained, not

¹ Recent investigations and theories that have to do with exceptions to the unvarying tetra-valence of carbon will not be considered in this book as they pertain to a more advanced study than is contemplated.

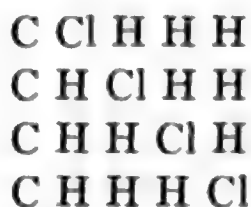
by saying that the valence of carbon has changed to two, but that *the valence of the carbon is not wholly satisfied*.

Methane a Saturated Compound.—Certain facts in connection with the relation of chlorine to methane indicate that the valence of carbon in organic compounds does not go above four, *i.e.*, that four is at least its maximum valence. When chlorine reacts with methane it is always by an act of substitution. Whenever a halogen atom enters the methane molecule it does so only when an atom of hydrogen has been given up. Under no known conditions does methane form compounds containing one or more halogen atoms *in addition* to the four hydrogen atoms already held by the carbon. We express this fact by saying that the carbon atom in methane is *saturated* by the four hydrogen atoms. Methane, then, is termed a *saturated compound*. We have spoken of the fact that the hydrocarbons are called paraffins because of their lack of affinity for other substances. Strictly speaking it is only those hydrocarbons which, like methane, are saturated to which the name paraffin applies. Methane is the simplest member of the *saturated hydrocarbons* or **paraffins**. The first idea then as to the structure of methane which the facts indicate is, that in it *the carbon atom is saturated*, or in other words, four hydrogen atoms fully satisfy the valence of carbon in methane.

Methane a Symmetrical Compound.—A second idea as to the structure of methane is gained likewise from a study of the chlorine or other halogen substitution products. The following fact has been established, *viz.*, that there is known *only one compound* each corresponding to the formulas for **mono-chlor methane**, **di-chlor methane** and **tri-chlor methane**. When mono-chlor methane is formed one atom of chlorine is substituted for one atom of hydrogen in the original methane molecule, and *the chlorine takes the same position as the substituted hydrogen*. If now the four hydrogen atoms in methane are in different relations to the carbon atom we should at least expect that sometimes one hydrogen and sometimes another would be substituted by the chlorine. If this were so then we should expect to have two or more mono-chlor methanes differing from each other in some way. The fact is that although mono-chlor methane has been made many times, and by different reactions, yet there has never been obtained a second compound corresponding to the formula CH_3Cl .

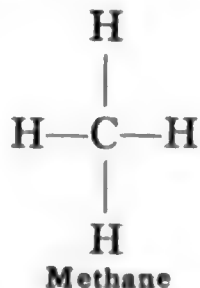
If we represent methane as $\text{C H}^1 \text{H}^2 \text{H}^3 \text{H}^4$ in which we have

numbered the different hydrogen atoms, then in case $H^1 H^2 H^3$ and H^4 are all different we should have

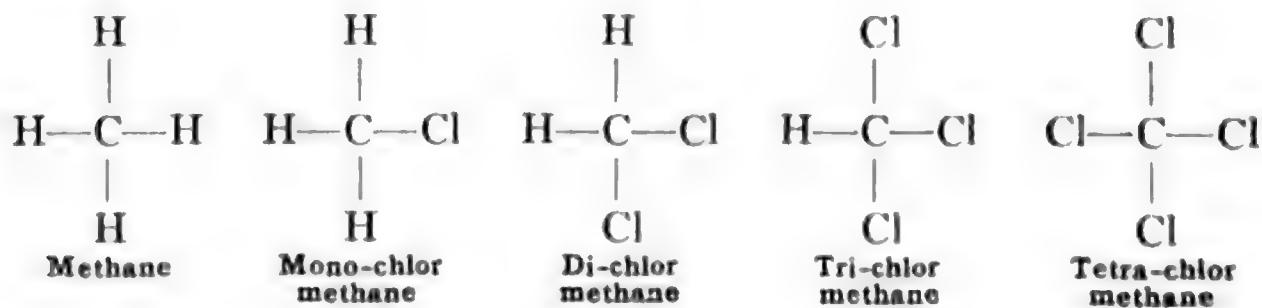


as the formulae for four different mono-chlor methanes. The *fact* that *only one mono-chlor methane is known* goes to show that $H^1 H^2 H^3 H^4$ are all alike and bear the same relation to the carbon atom in the methane molecule. In addition to this indirect proof it has been shown that each of the four hydrogen atoms in methane may be replaced one and only one at a time by one chlorine atom, and the four resulting mono-chlor methanes are *identical*. In methane, therefore, the four hydrogen atoms are alike in their relation to the carbon atom, or in other words *the methane molecule is symmetrical*.

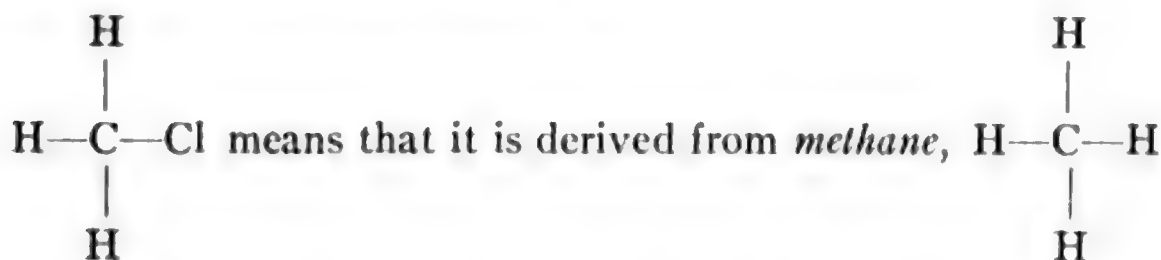
Structural or Constitutional Formula.—To represent a compound whose formula is CH_4 in a way that will indicate the two facts just discussed, viz., *saturation of the carbon atom*, and *symmetrical arrangement of the four hydrogen atoms*, the following graphic formula is used:



This means that methane is CH_4 , a *saturated*, *symmetrical* compound, in which carbon is *tetra-valent*, and all of the hydrogens are alike. It should be emphasized again that such a formula, which we call a *structural* or *constitutional formula*, does not represent the arrangement of the atoms in space, but is simply a plane representation of the most important facts in regard to methane as shown by definite reactions. The structural formulae for methane and the four chlor methanes are then as follows:

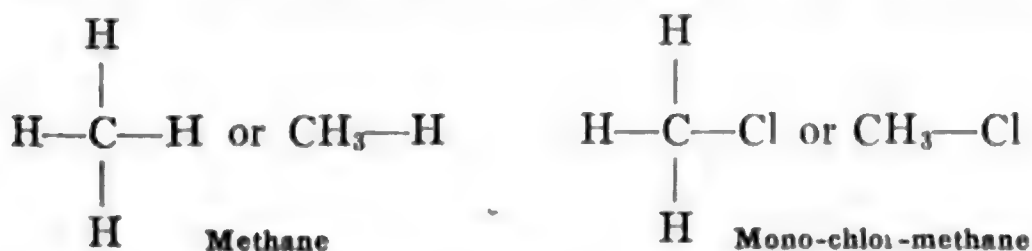


It is very important to grasp at the beginning the full significance and likewise the limitations of these structural formulas. To repeat; the formula for **mono-chlor methane**, viz.,



by substituting *one chlorine atom for one hydrogen atom*. The *four hydrogen atoms being alike* it makes no difference in which position we place the chlorine. Also, *carbon is tetra-valent*, and methane and mono-chlor methane are *saturated* compounds in which each of the four hydrogen atoms or each of the hydrogen atoms and the chlorine atom are joined directly to the carbon atom. The formula is a *plane representation of these facts, and indicates nothing as to space relations*.

When chlorine is substituted for hydrogen in methane and mono-chlor methane is obtained, we may assume as probable that one chlorine atom first removes hydrogen from the methane molecule, and then a second chlorine atom unites with the residue of methane. When one hydrogen is removed from methane we have left the residue (CH_3-), *i.e.*, CH_4 may be written CH_3-H . In mono-chlor methane, then, the chlorine may be considered as united to the residue (CH_3-) which as a group possesses the one valence of the carbon left unsatisfied by the one lost hydrogen. By our structural formulas we may represent the relations between methane and mono-chlor methane as



As in mono-chlor methane chlorine is thus represented as joined to the group (CH_3-), so in all mono-substitution products of methane a monovalent element or group is joined to the monovalent group (CH_3-). A general formula, therefore, for all mono-substituted methanes may be written, CH_3-X ; X being any mono-valent element or group.

Radical.—It has been found that there is a large series of compounds all of which contain this group (CH_3-) and all of which are derived

from or related to methane. Furthermore, not only this group, but many other groups act in a similar way, forming different series of compounds, each series containing a common group. *A group of elements thus running unchanged through a series of compounds has been called a radical.*

The theory of radicals was held for some time in a general and rather indefinite way, both as applied to inorganic and organic compounds, before the year 1832. But in this year two chemists whose names are always associated, and both of whom brought about great advances in organic chemistry, viz., **Liebig** and **Wöhler**, published a joint investigation on "*The Radical of Benzoic Acid.*" In this investigation they showed that a group of elements ($\text{C}_7\text{H}_5\text{O}-$), according to our present atomic weights, was present in a series of some nine compounds, which were readily transformable into each other. As a result of this classical investigation, and others which followed, the idea of an organic radical became more and more firmly established. A radical came to be considered as a group of several elements, in a compound, joined together more securely than the rest of the compound, and which remains unchanged as a constituent of a series of related compounds. In itself it may be replaced by other elements or groups, and is also possible of undergoing substitution, thereby, however, becoming a new radical. Hardly any theory that has been advanced has had a more powerful and fruitful effect than this theory of radicals, and it has been one of the great ideas which has enabled chemists to understand the character of organic compounds and to change a miscellaneous group of unrelated compounds into a definite system of wonderfully related ones. **Liebig** himself termed organic chemistry the "*chemistry of the compound radical.*" In any series of compounds, and every compound was soon shown to belong to a more or less extended series, the constant unit which was the basis of relationship was the radical. The other part of the compound was alterable at will through ordinary laboratory reactions, so that the transformation of one compound into others was readily brought about and relationships thus established. Compounds took their names from those of the radicals present in them.

Methyl.—The radical (CH_3-) is known as **methyl** and the compounds containing it are termed **methyl** compounds. Similar names have been given to all radicals by taking a part of the word used as the name of the compound from which the radical is derived, and adding the

termination *yl*. In almost all cases the radical is not known as such and has not been isolated. *R* is used to denote any radical, usually one derived from a hydrocarbon.

Methyl Halides.—The mono-halogen substitution products of methane, of which we have been speaking, are known by this new system of names as methyl compounds so that we have the two sets of names for the same substances, both of which are correct and either of which expresses the relationship to methane.

Mono-chlor methane	CH_3Cl	Methyl chloride
Mono-brom methane	CH_3Br	Methyl bromide
Mono-iodo methane	CH_3I	Methyl iodide

The general name being:

Mono-halogen methanes	Methyl halides
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These two ideas or theories of *substitution* and of *radicals* and the facts in regard to methyl compounds enable us to understand the relationship between methane and the hydrocarbon next higher to it in the series.

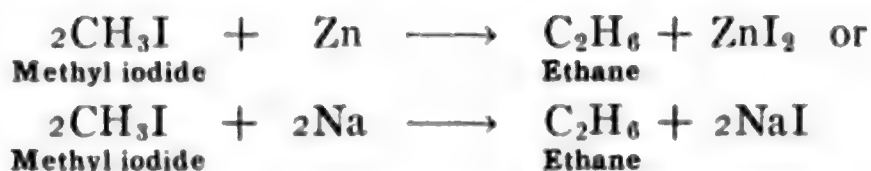
Ethane C_2H_6

This compound is similar to methane in many ways. It is a gas, slightly heavier than air, having a density of 15.0. It is colorless and odorless and burns with a flame somewhat more luminous than that of methane. It is found in nature in sources similar to those of methane, as in natural gas and in petroleum. Like methane it is chemically inactive and a hydrocarbon of the paraffin series.

Ethane a Saturated Compound.—Like methane, ethane is unable to take up chlorine or any other element without at the same time losing hydrogen and forming a substitution product. This is the character we term *saturation* and in methane we say that four hydrogens or any four monovalent elements are all that carbon with its tetra-valence can hold. Now in ethane these same facts are true. Analysis, however, shows ethane to have the composition C_2H_6 and, according to our usual manner of regarding union between atoms, if carbon remains tetra-valent, as we have previously stated, only six of a total of eight bonds or valences are satisfied. How, then, have these facts been brought into harmony?

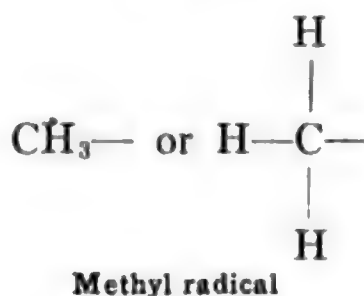
Synthesis of Ethane.—By a consideration of the synthetic preparation of ethane from methane we are able to understand its structure in

accordance with our ideas of the *tetra-valence* of carbon, and with the fact that it acts as a *saturated* compound. When **mono-iodo methane**, which we have also called **methyl iodide**, and which name will usually be used, is treated with zinc or sodium, **ethane** is formed, two molecules of methyl iodide yielding one of ethane. In this reaction the iodine is taken by the zinc or sodium and we may write the reactions:

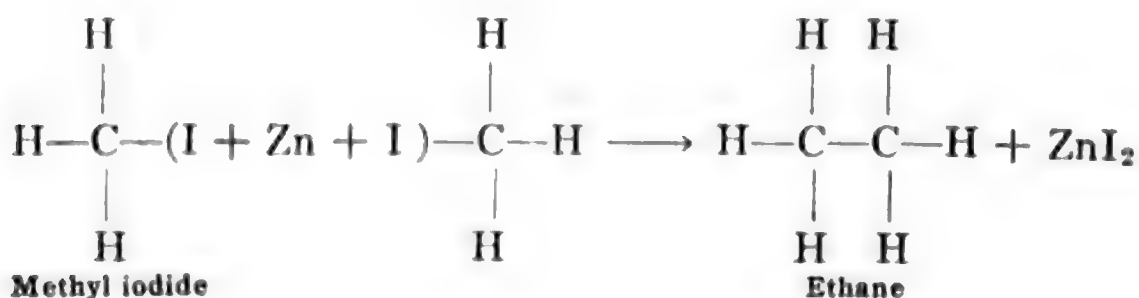


These two reactions are known by the names of the men who discovered them. The first one, with zinc, is known as the **Frankland Reaction** and will be spoken of again (page 76). The second, with sodium, is known as the **Wurtz Reaction**.

The radical methyl which, as we stated, does not exist free, is represented as having a valence of one.

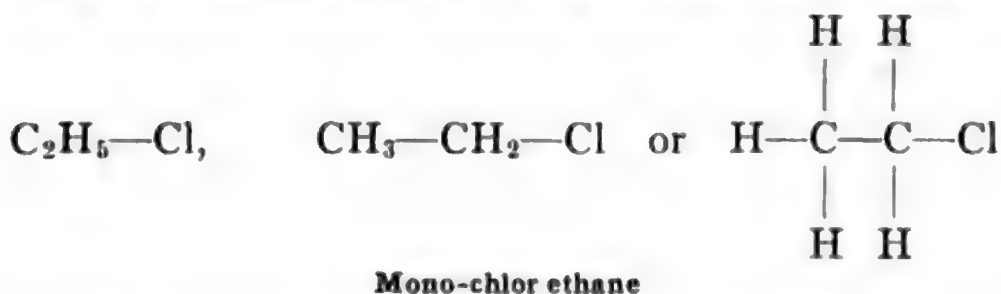


One of the four bonds of the carbon is left free. In methane this free bond is satisfied by another hydrogen atom; in methyl chloride or iodide by one of chlorine or iodine, making in each case a saturated compound. When, therefore, two molecules of methyl iodide each lose their iodine to zinc or sodium we have left the two methyl radicals with this fourth valence of each carbon unsatisfied. These two free valencies *satisfy each other*, and we have the *two methyl radicals united*, just as we believe two free atoms unite to form a molecule. We may write the reaction then:

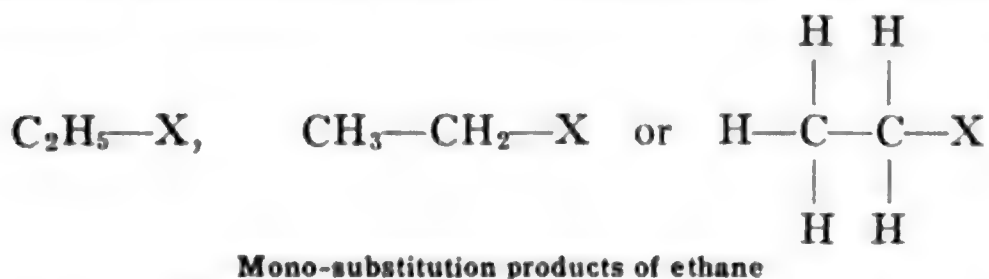


Ethane may be considered then as **di-methyl**, or as **methyl methane**, *i.e.*, methane in which a methyl radical ($\text{CH}_3\cdot$) has been substituted for one hydrogen atom. In it three of the valencies of each carbon atom are satisfied by hydrogen atoms while the fourth valencies of the two carbon atoms mutually satisfy each other. The two carbon atoms thus become directly linked together. In such a compound both of the carbon atoms have all four of their valencies satisfied, and the compound is, therefore, saturated. This formula then agrees both with the fact that ethane acts as a *saturated compound* and with the theory that *carbon is tetra-valent* and, furthermore, it is the logical explanation of the reaction by which it is formed from methyl iodide.

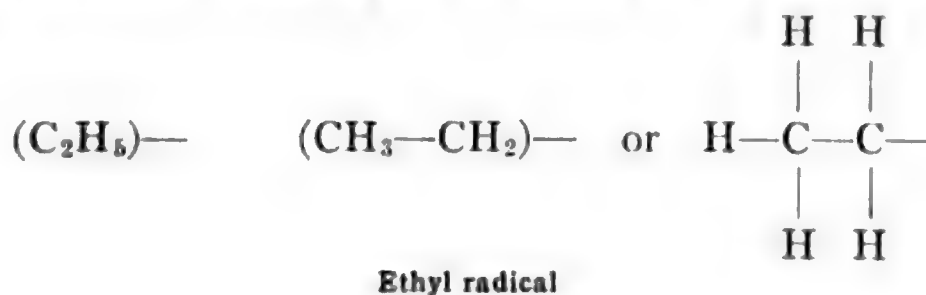
The next question which arises in regard to ethane is; is ethane like methane in being symmetrical, *i.e.*, are all of the hydrogen atoms alike in their relation to the carbon atoms and to each other? The same kind of facts which established this point in regard to methane are also true of ethane, *viz.*, *only one mono-chlor ethane is known*. We thus conclude that *all six hydrogen atoms in ethane are alike*, and no matter which one is substituted by chlorine the product is always the same. We may write the structural formula for mono-chlor ethane then:



The general formulas for mono-substitution products of ethane are:



The radical of ethane is analogous to *methyl* and is known as *ethyl*.



One other fact should be noticed here. We see that ethane, C_2H_6 , differs in composition from methane, CH_4 , in having *one carbon and two hydrogens* more, *i.e.*, by (CH_2) . This is clearly understood when we remember ~~that~~ in making ethane from methane we have taken away one hydrogen and put in its place (CH_3) or we have really added (CH_2) .

Propane, Butane, Pentane, Hexane and the Higher Saturated Hydrocarbons

We have now laid the foundation for considering the other hydrocarbons which are similar to methane and ethane and for understanding an interesting relationship which makes of them a family or series. At the present time about fifty hydrocarbons are known which resemble methane and ethane in being *saturated, stable, inactive* compounds, and to which the name *paraffin* strictly applies. Some of these hydrocarbons with their empirical formulas and a few of their physical constants are given in the following table:

Several striking things will be noticed in regard to the hydrocarbons given in this table as to their (a) physical properties, (b) composition, (c) structure or constitution. It will be noted that the compounds are arranged in the order of their carbon content.

Physical Properties.—On examining the physical properties of the hydrocarbons given it will be seen that these properties vary in a more or less progressive and constant manner, usually increasing as we go up the series. The four lower members from methane to butane are gases at ordinary temperatures, the next thirteen are liquids below 25° , while the remainder are solids. This can be seen more clearly by examining the three physical constants given, in each of which, especially the melting point and boiling point, there is a more or less uniform increase from the first member to the highest.

Composition and Constitution.—A similar constant progressive change is seen in the composition. Each compound differs from the one immediately preceding it by the constant amount CH_2 . As will be recalled this was spoken of in the case of ethane as being the difference in composition between it and methane. It was shown then that this is in accord with its synthesis from methyl iodide and sodium, **ethane** being **methyl methane** (p. 16).

Not only, however, does this synthesis make plain to us the constitution of ethane and its relation to methane, but the reaction is a general one for the synthesis of hydrocarbons and for establishing their

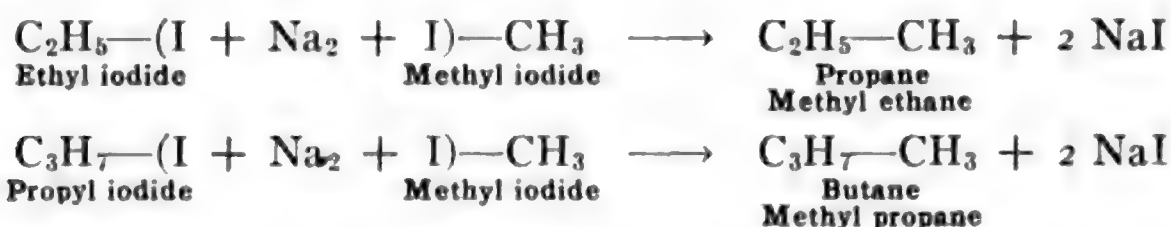
TABLE I.—HOMOLOGOUS SERIES OF SATURATED HYDROCARBONS (PARAFFINS)
General Formula C_nH_{2n+2}

Name	No. of isomers known	Empirical formula	Melting point (M.P.)	Boiling point (B.P.)	Specific gravity (Sp. Gr.)
				At 760 mm.	
Methane.....	..	CH_4	-186°	-152°	0.415 (-164°)
Ethane.....	..	C_2H_6	-90°	
Propane.....	..	C_3H_8	-37°	
Butanes.....	2	C_4H_{10}			
Normal butane.....	..	C_4H_{10}	$+1^\circ$	0.60 (0°)
2-methyl propane.....	..	C_4H_{10}	-11.15°	
Pentanes.....	3	C_5H_{12}			
Normal pentane.....	..	C_5H_{12}	36°	0.6337 (15°)
2-methyl butane.....	..	C_5H_{12}	31°	0.6271 (15°)
2-2-di-methyl propane.....	..	C_5H_{12}	-20°	9°	
Hexanes.....	5	C_6H_{14}			
Normal hexane.....	..	C_6H_{14}	69°	0.6654 (15°)
3-methyl pentane.....	..	C_6H_{14}	64°	0.6765 (20.5°)
2-methyl pentane.....	..	C_6H_{14}	62°	0.6766 (0°)
2-3-di-methyl butane.....	..	C_6H_{14}	58°	0.6680 (17.5°)
2-2-di-methyl butane.....	..	C_6H_{14}	49.6°	0.6488 (20°)
Normal heptane.....	5	C_7H_{16}	98.4°	0.683 (20°)
Normal octane.....	2	C_8H_{18}	125°	0.702 (20°)
Normal nonane.....	3	C_9H_{20}	-51°	150°	0.718 (20°)
Normal decane.....	6	$C_{10}H_{22}$	-31°	173°	0.730 (20°)
Normal undecane.....	1	$C_{11}H_{24}$	-26°	195°	0.774 (M.P.)
Normal dodecane.....	1	$C_{12}H_{26}$	-12°	214°	0.773 (M.P.)
Normal tridecane.....	1	$C_{13}H_{28}$	-6°	234°	0.775 (M.P.)
Normal tetradecane.....	1	$C_{14}H_{30}$	$+4^\circ$	252°	0.775 (M.P.)
Normal pentadecane.....	1	$C_{15}H_{32}$	10°	270°	0.776 (M.P.)
Normal hexadecane.....	2	$C_{16}H_{34}$	18°	287°	0.775 (M.P.)
Normal heptadecane.....	1	$C_{17}H_{36}$	22°	303°	0.777 (M.P.)
Normal octadecane.....	1	$C_{18}H_{38}$	28°	317°	0.777 (M.P.)
Normal nonadecane.....	1	$C_{19}H_{40}$	32°	330°	0.777 (M.P.)
				At 15 mm.	
Normal eicosane.....	1	$C_{20}H_{42}$	37°	205°	0.778 (M.P.)
Normal heneicosane.....	1	$C_{21}H_{44}$	40°	215°	0.778 (M.P.)
Normal docosane.....	1	$C_{22}H_{46}$	44°	224°	0.778 (M.P.)
Normal tricosane.....	1	$C_{23}H_{48}$	48°	234°	0.779 (M.P.)
Normal tetracosane.....	1	$C_{24}H_{50}$	51°	243°	0.779 (M.P.)
Normal hexacosane.....	1	$C_{26}H_{54}$	44°		
Normal heptacosane.....	1	$C_{27}H_{56}$	60°	270°	0.780 (M.P.)
Normal hentriacontane.....	1	$C_{31}H_{64}$	68°	302°	0.781 (M.P.)
Normal dotriacontane.....	1	$C_{32}H_{66}$	70°	310°	0.781 (M.P.)
Normal pentatriacontane.....	1	$C_{35}H_{72}$	75°	331°	0.782 (M.P.)
Normal hexacontane.....	1	$C_{60}H_{122}$	101°		

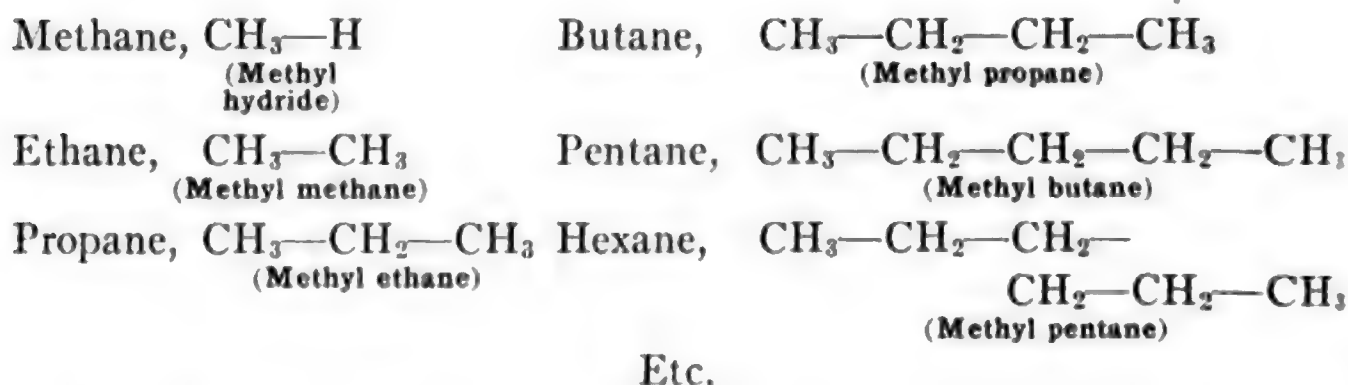
constitution. By means of it the methyl radical may be linked to any other radical, a new hydrocarbon thereby resulting.



Propane and Butane.—In this way **propane**, C_3H_8 , has been made from **ethyl iodide**, **methyl iodide** and sodium and it must therefore be **methyl ethane**. Also **butane**, C_4H_{10} , similarly made from **propyl iodide**, **methyl iodide** and sodium, is **methyl propane**. The reactions are as follows:¹



This general method of synthesis has been applied to each member of the methane series with the result that *each hydrocarbon has been proven to be the methyl substitution product of another hydrocarbon containing one less carbon atom*. We have then for the successive members of the series a continually elongating chain of carbon groups, each group being a residue of methane. For the first six members the formulas are as follows:



A-cyclic or Open Chain Compounds.—Such compounds, because their structure is that of a chain of carbon groups, the ends of which chain do not unite to form a ring, are known as *open chain* or *a-cyclic* compounds in distinction from *closed chain* or *cyclic* compounds which we shall meet with in the second part of our study. Their structure explains also the general formula for the series as given at the top of the table, viz., C_nH_{2n+2} . Each carbon atom excepting the two end

¹ In these two reactions propane and butane are not the only products, other hydrocarbons being also formed. See synthesis of butane and hexane (p. 24 et seq.).

ones, is linked to two hydrogen atoms. The two end carbon atoms each having three hydrogens makes the total number of hydrogen atoms two more than twice the carbon atoms, *i.e.*, if n equals the number of carbon atoms $2n + 2$ will equal the number of hydrogen atoms. Therefore, any hydrocarbon of this series will have the formula C_nH_{2n+2} .

Homologous Series.—A series of compounds, the members of which differ in composition by a constant amount, and whose physical constants change uniformly, constitute what has been termed an *homologous series*. This particular series which we are discussing is known as the *homologous series* of the *saturated* or *paraffin hydrocarbons*, which are also *open chain* or *a-cyclic* compounds, the general formula of which is C_nH_{2n+2} .

Names.—The names of the different hydrocarbons are similar and are in harmony with the idea of an homologous series. The common termination *ane* is given to all and, above the fourth member, a Greek numerical prefix indicates the number of carbon atoms in the molecule. The five-carbon compound is **pent-ane**, the six carbon **hex-ane**, etc. The first four members have special non-numerical prefixes as **meth-ane**, **eth-ane**, **prop-ane** and **but-ane**. Similarly the radicals of each hydrocarbon simply take the termination *yl* in place of *ane*, thus, *but-yl*, *pent-yl*, *hex-yl*, etc.

Alkyl.—The general name for a radical of this series is *alkyl*. A *halogen alkyl* or *alkyl halide* is thus a halogen substitution product of any paraffin hydrocarbon, or it is composed of a paraffin or alkyl radical linked to a halogen atom. The general formula for an *alkyl radical* is (C_nH_{2n+1}) .

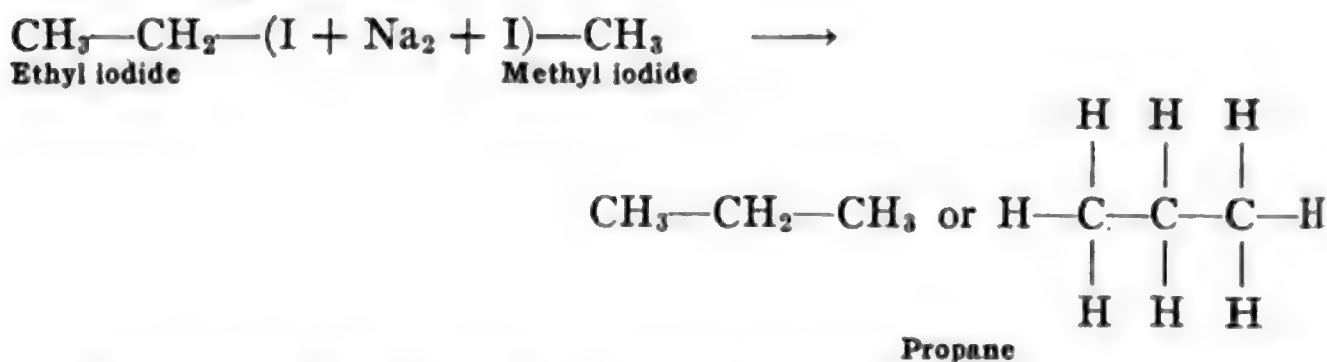
Isomerism.—We come now to a consideration of one of the most interesting phenomena of organic chemistry, *viz.*, *isomerism*. In speaking of ethane, we showed how the fact that only one compound is known of the formula C_2H_5-Cl , **ethyl chloride**, proves that in ethane, as in methane, all of the hydrogen atoms are alike in their relation to the carbon atoms. When, now, we study the third hydrocarbon, **propane**, we find a new fact which must be explained. **Mono-iodo propane**, which is the mono-iodine substitution product of propane, usually known as **propyl iodide**, has by analysis the formula C_3H_7-I ; but, there are known *two* compounds having the same formula but distinctly different properties. Both of these compounds are prepared

from propane by substituting one iodine atom for one hydrogen atom and each of them is therefore **propyl iodide**. The difference in the physical properties of these two compounds may be seen from the following:

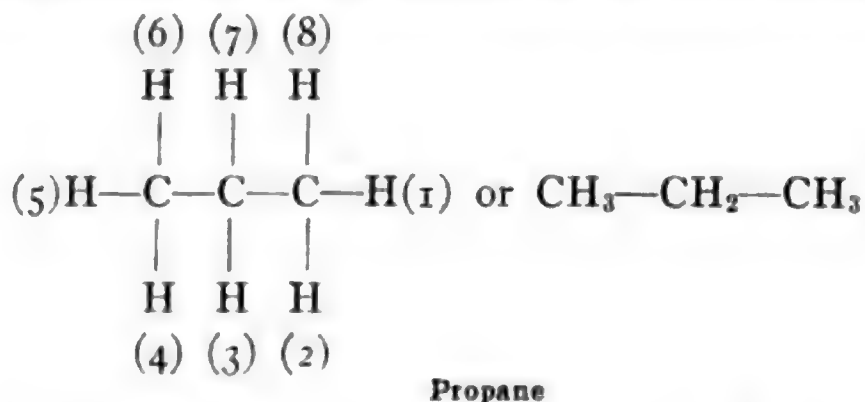
	B.P.	Sp. Gr.
Compound A.....	102.5	1.78
Compound B.....	89.0	1.74

How then can we explain the existence of two propyl iodide compounds of the same molecular formula but different properties?

The structural formula for propane, based upon its synthesis from **ethyl iodide** and **methyl iodide** in the presence of sodium, is as shown in the following reaction:

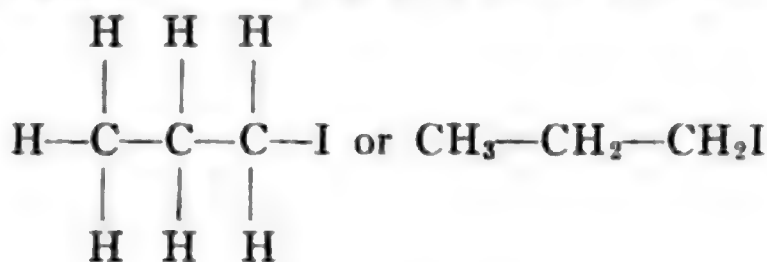


There are eight hydrogen atoms in the propane molecule, and if propane is a symmetrical compound and all of the hydrogen atoms are alike in relation to the carbon atoms it should make no difference which hydrogen we substitute by iodine. The *fact* as just stated, however, is that *two propyl iodide compounds exist*. There must then be two hydrogen atoms in the propane molecule, each of which is in a different relation to the carbon atoms. The fact again is that *only two* propyl iodide compounds are known; therefore, there are *only two hydrogen atoms*, or two sets of hydrogen atoms, in propane that are different. On examination of the structural formula for propane, viz.,



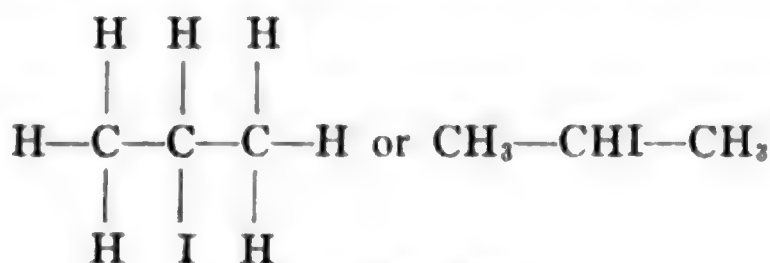
in which for convenience we have numbered the hydrogen atoms, we see that hydrogen atoms 1, 2, 4, 5, 6, 8, are apparently alike and are

each linked to a carbon atom which is linked to *two other hydrogen atoms*, and to *one other carbon atom*. The hydrogen atoms 3 and 7, however, are linked to a carbon atom which is linked to *one other hydrogen atom* and to *two other carbon atoms*. If we substitute iodine for one of the hydrogen atoms 1, 2, 4, 5, 6, 8, we will have:



Propyl iodide, A

If the iodine is substituted for one of the hydrogen atoms, 3 or 7, we have:



Propyl iodide, B

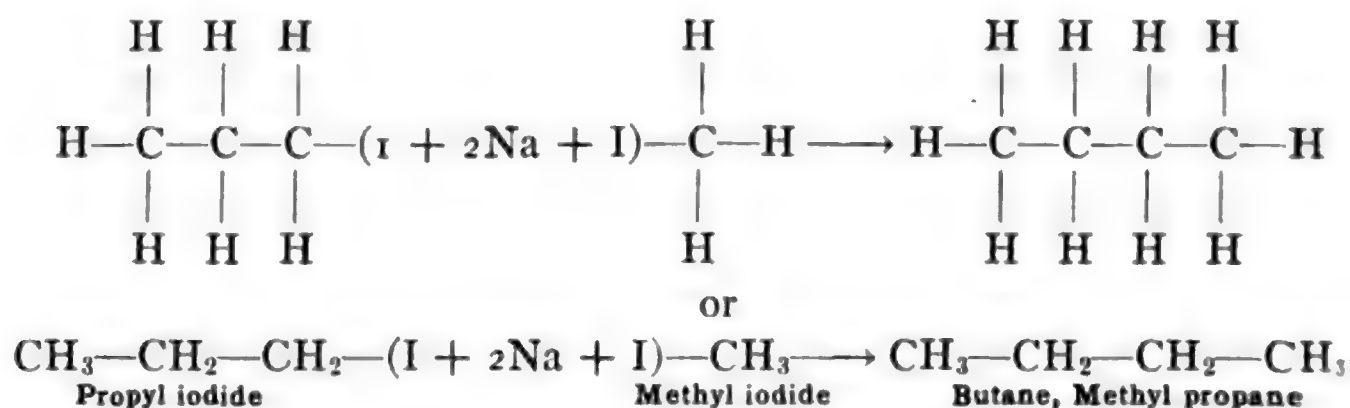
If the hydrogen atoms 2, 4, 5, 6 and 8 are like 1 and the hydrogen atom 7 is like 3, then only these two different compounds would be possible. *The fact that two and only two* propyl iodides are known leads to the conclusion that in propane there are two sets of hydrogen atoms and only two sets, and that substitution of iodine for any one of the hydrogens in the two sets will yield two different propyl iodides. Also, the fact that two different mono-substituted propanes are known in each of the classes of substitution products, viz., the *chlorine, bromine, iodine, methyl, hydroxyl, amino*, etc., strengthens our belief in this idea.

Structural Isomerism.—The phenomenon of the existence of two or more compounds possessing the same composition and empirical formula but which show different physical and chemical properties is known as *isomerism*, and the compounds themselves are called *isomeric compounds, isomers* or *isomerides*. That the difference is in the structure or constitution characterizes them further as *structural isomers* and the phenomenon as *structural isomerism*. The word isomerism was suggested by **Berzelius** in connection with **Wöhler's** synthesis of *urea* (p. 429).

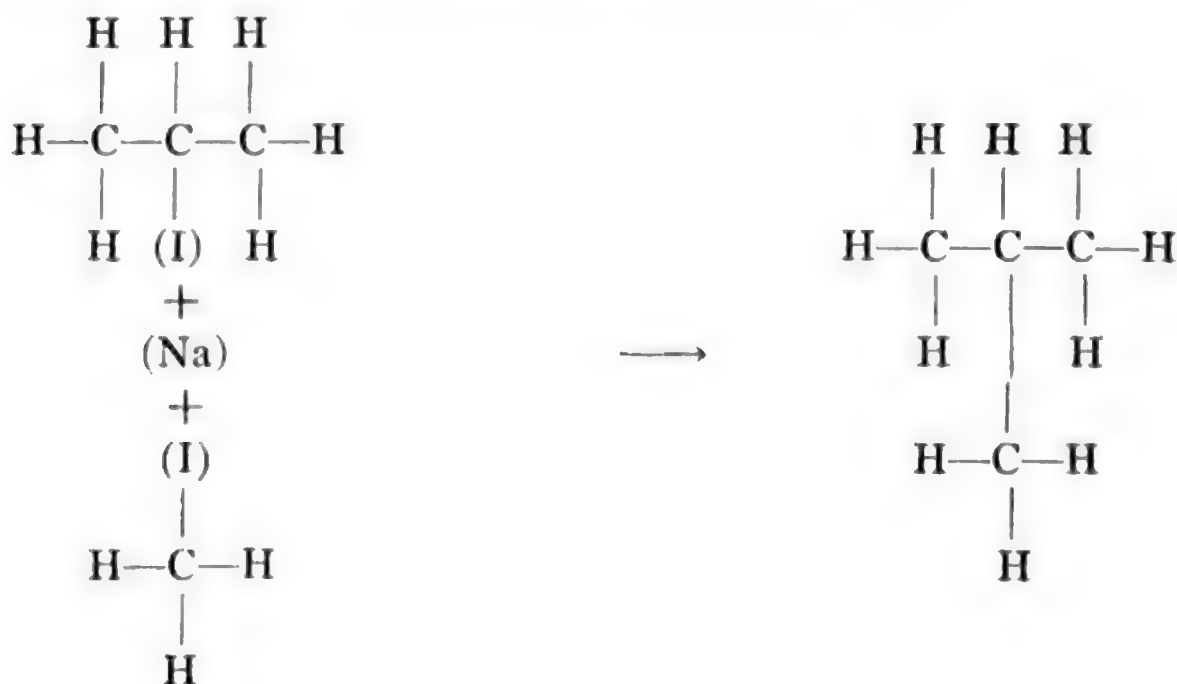
Isomeric Hydrocarbons, Butanes.—Having explained the phenomenon of isomerism by means of the isomeric propyl iodides we shall

now see how the idea is applied in the case of isomeric hydrocarbons. We have shown by the synthesis of the hydrocarbons (pp. 16–20) that **ethane** is **methyl methane** and **propane** is **methyl ethane** so **butane** is **methyl propane**. Methyl propane, being a methyl substituted propane is, like all mono-substituted propanes, possible of existence in two isomeric forms exactly similar in their structure to the two propyl iodides, **iodo propanes**. We should, therefore, expect to find two isomeric **mono-methyl propanes** or **butanes**. This is the *fact*, *two butanes are known* possessing the same composition or empirical formula, but with different properties as given in the table (p. 19), one boiling at $+1^\circ$ and the other at -11.15° .

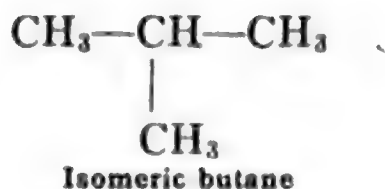
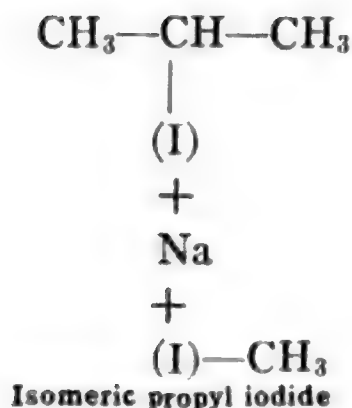
Synthesis of the Two Butanes.—The *two isomeric propyl iodides*, by means of the **Wurtz** and **Frankland** reactions, yield the *two isomeric butanes*, the constitution of which must, therefore, be as shown in the following reactions:



The isomeric propyl iodide yields the isomeric butane

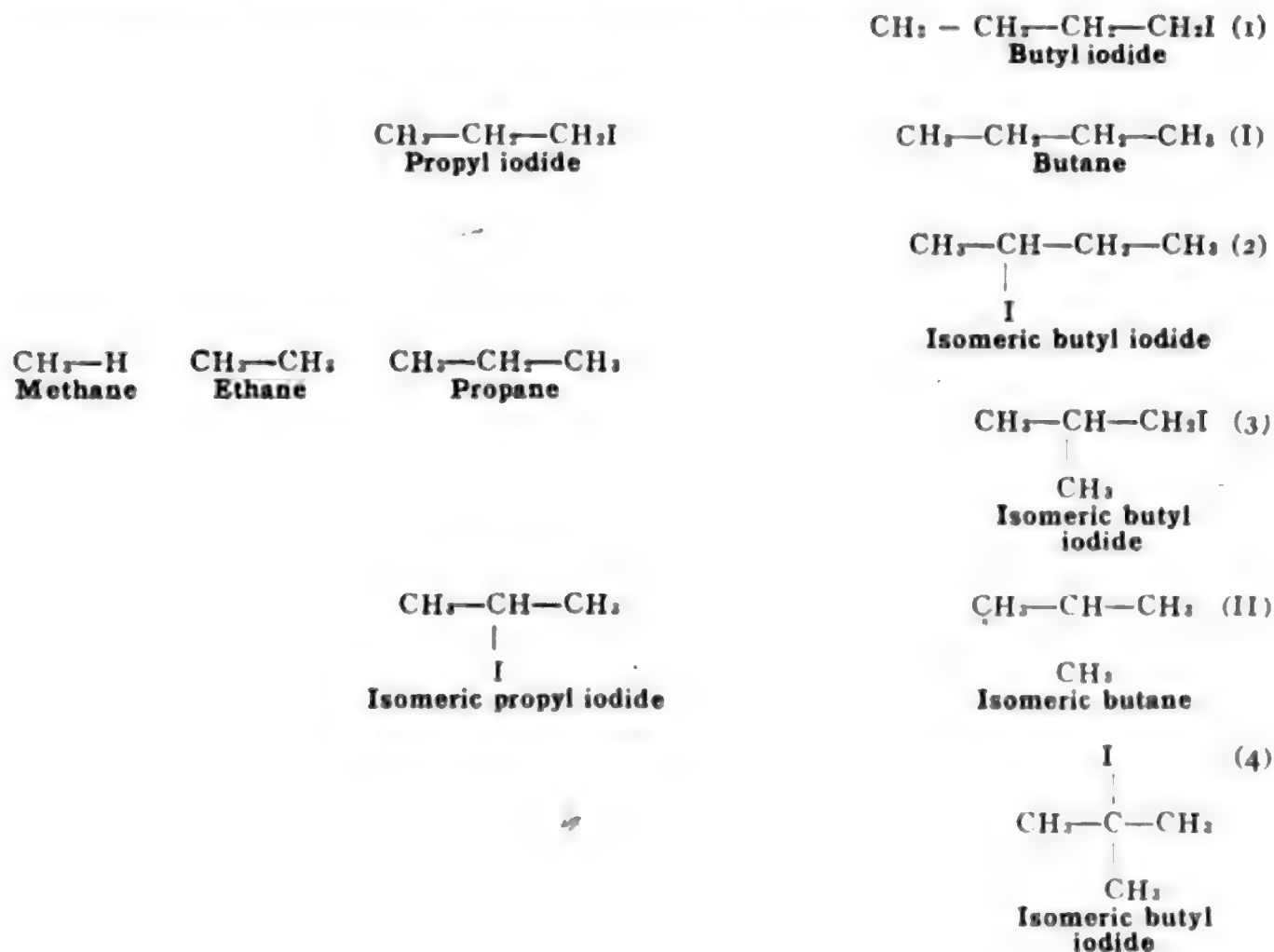


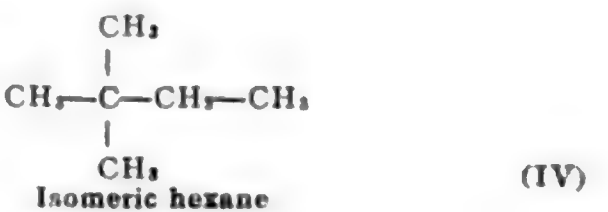
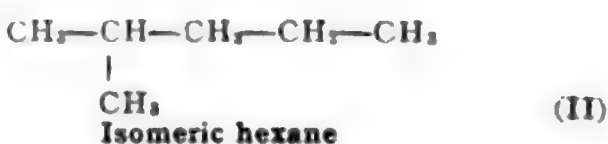
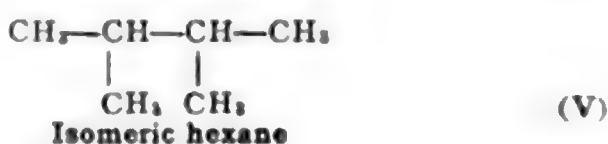
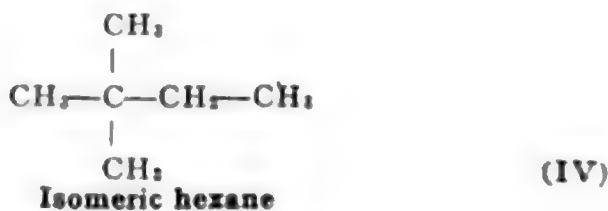
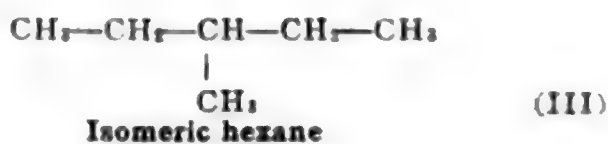
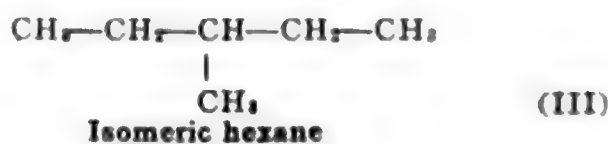
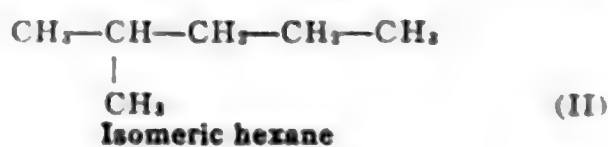
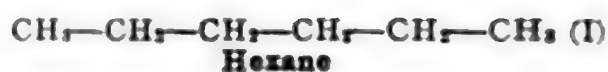
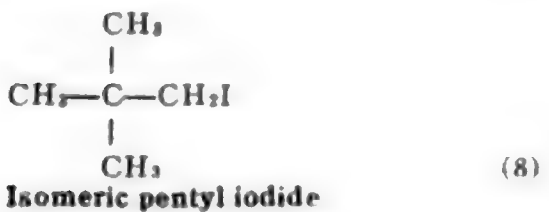
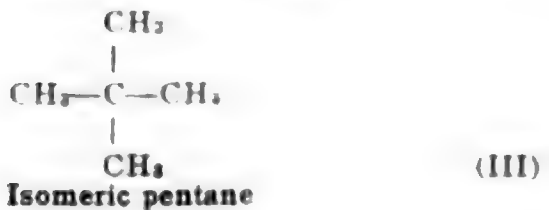
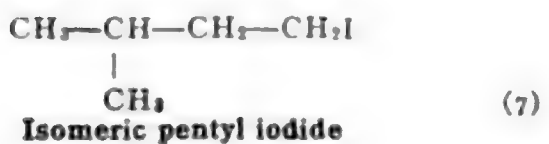
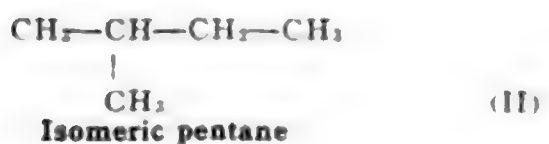
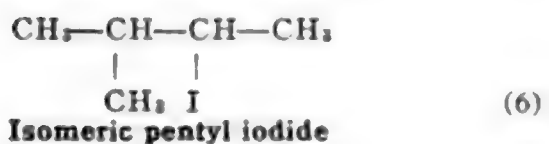
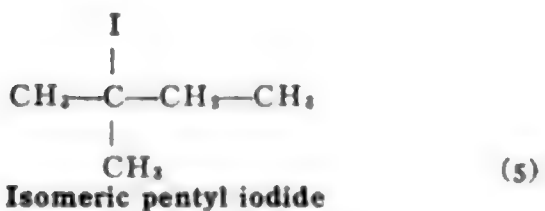
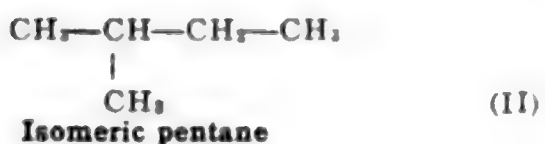
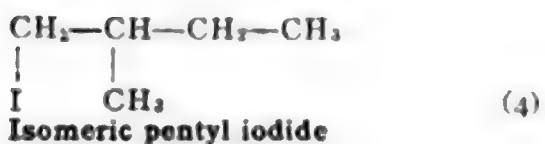
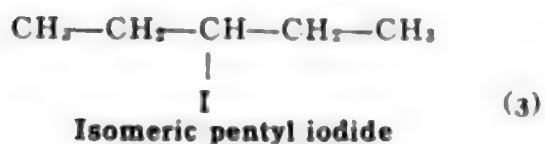
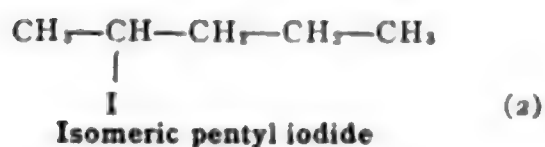
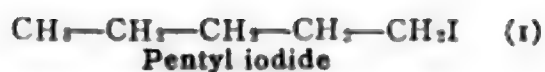
or



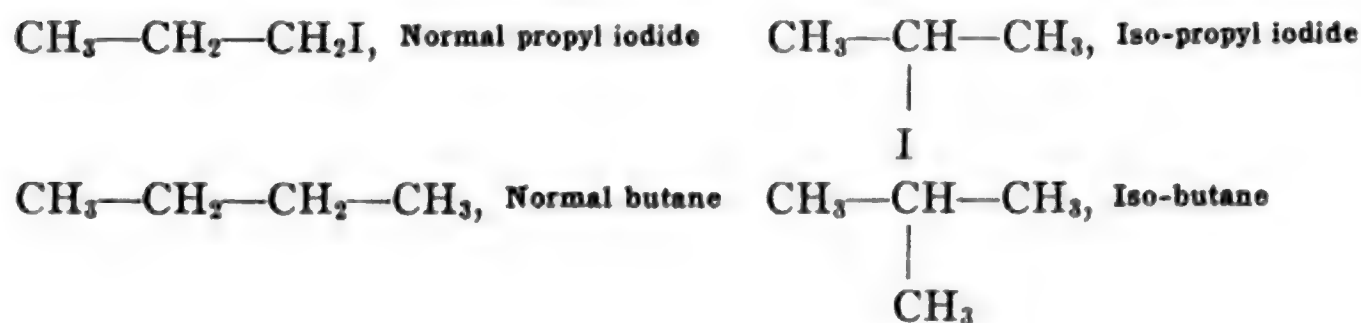
Pentanes and Hexanes.—In exactly the same way in which we have explained the isomerism in the case of the propyl halides and butanes we are able to explain that of the **pentanes** and **hexanes**. The number of possible isomeric hydrocarbons naturally increases as the number of carbon atoms increases. *Three isomeric hydrocarbons of the formula C_5H_{12} are possible and three are known, and five of the formula C_6H_{14} , all likewise being known.*

The following schematic representation of the relation between the hydrocarbons from methane to hexane may help to make clear the continually increasing number of isomers possible.



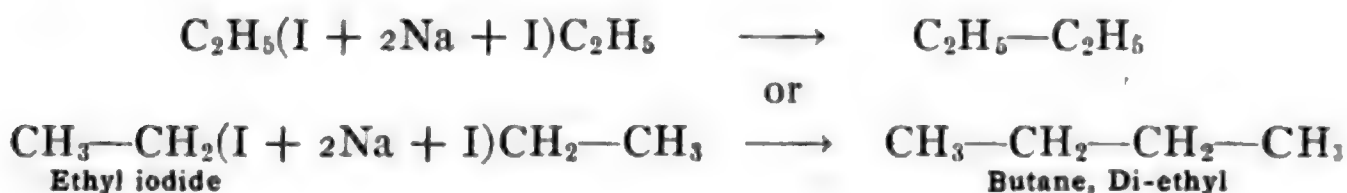


Normal and Iso Compounds.—The hydrocarbons of this series have been spoken of as belonging to the general class of *a-cyclic* or *open chain* compounds. By examining the formulas of the isomeric butanes, pentanes and hexanes on the preceding page it will be seen that, while they are all open chain compounds, *i.e.*, no two carbon atoms are linked in such a way as to form a closed ring, yet this chain is more or less branched in all cases except in one compound of each isomeric group. *One butane, one pentane* and *one hexane* each has a formula which may be characterized further as a *straight* open chain while the others are all *branched* open chains. The name *normal* has been applied to these straight chain formulas, and the hydrocarbon which can be shown to have such a formula is known as the *normal* hydrocarbon. In case there is only one other isomeric compound, as with the butanes or the propyl halides, it is often called simply the *isomeric* or, abbreviated, the *iso* compound. Therefore

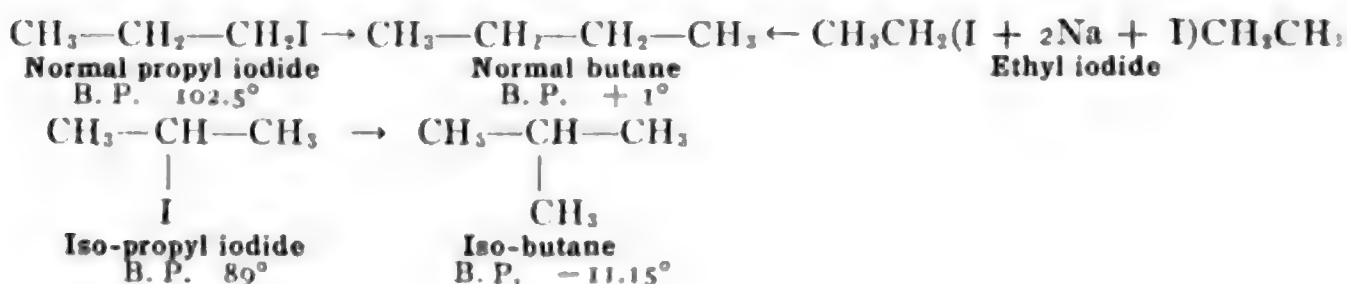


The question now arises, how may we determine which one of the various formulas, in the case of the five hexanes for instance, is to be assigned to each individual compound of definite physical properties? To which one of the butanes, pentanes and hexanes do we assign the straight chain formula or the name normal? In the case of the butanes the answer and the reason for it are found in a new synthesis of one of the butanes. We have given one synthesis of the two butanes, *viz.*, from **propyl iodide** and **methyl iodide**. As one propyl iodide yields one butane and the other yields the isomeric butane, we know that one of the two isomeric butanes must have the straight chain or normal formula. But we do not know whether the propyl iodide from which the butane boiling at $+1^\circ$ is prepared, is really the one possessing the normal or the iso formula. Therefore, it will be seen that the relationship between the isomeric propyl iodides and the isomeric bu-

taness explains nothing as to which formula belongs to which compound until we have some proof that either one of the butanes or one of the propyl iodides is in fact the one which must have the normal formula. Now butane may be synthesized in another similar way. If **ethyl iodide** alone is treated with sodium or zinc we obtain *only one butane* as the product. This synthesis proves that this particular butane is **di-ethyl** just as on page 16 we show why ethane is to be considered as **di-methyl**.

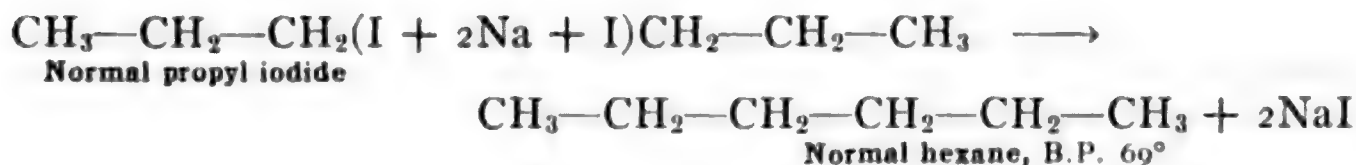


Now the only way in which two ethyl radicals may be linked together is as a straight chain compound, and therefore *the* butane so made must be the one with the straight chain formula, and the one which we must call *normal*. The *fact* is that this synthesis always yields *the butane with boiling point + 1°*. This, then, is *normal butane* and the one boiling at -11.15° is *iso-butane*. The synthesis of the two butanes from the two propyl iodides may now be used to prove which of the latter is the *normal* and which the *iso* compound. The butane which we have just proven to be *normal butane* and which boils at $+1^\circ$ is always obtained from the propyl iodide *with boiling point* 102.5° , which must therefore be **normal propyl iodide**. Similarly **iso-butane** is obtained from the propyl iodide *boiling at* 89° , and this must be **iso-propyl iodide**. We have, then, the following relationship established and the compounds with the definite boiling points as given must have the constitution assigned to them.



Analogous to the synthesis of normal butane from sodium and ethyl iodide alone is the fact that **normal propyl iodide** *alone* with sodium

yields a hexane, which boils at 69° and which by this synthesis must be **normal hexane** :

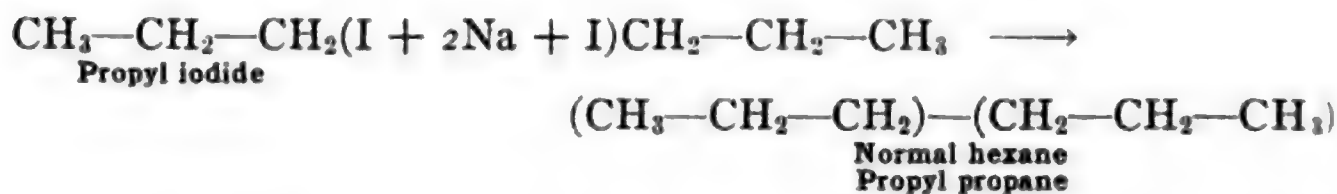


This same hexane may also be prepared from a pentyl iodide, and as the hexane has the normal structure the pentyl iodide from which it is made must similarly be **normal pentyl iodide**, and its hydrocarbon is **normal pentane**. By a series of such reactions the exact constitution of each *butane*, *pentane* and *hexane* and their iodides has been established. It has been found that in each group of isomeric hydrocarbons the *normal* compound is the one having the highest boiling point. The normal hydrocarbons themselves form a gradually ascending series as indicated by their boiling points, while each group of isomeric hydrocarbons forms a gradually descending series. These two facts of an *ascending series of normal compounds* and a *descending series of each group of isomeric compounds* have been found to be true, not only for the hydrocarbons, but for each series of substitution products of these hydrocarbons. This emphasizes in a striking way the family or series relationship. The homologous nature of each such series of organic compounds is thus seen to be something fundamental which finds its most probable explanation in our conception of structure or constitution as we have discussed it.

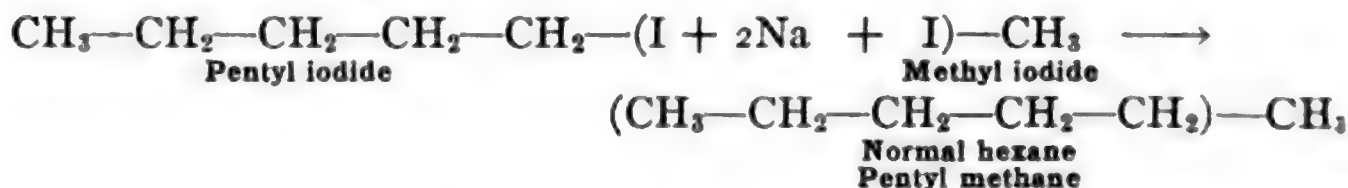
Names of Isomers.—As we have just stated, the names of the two propyl iodides and of the two butanes may be simply *normal* and *iso*. In each group of isomers where only two are possible these two names are sufficient to characterize them as structurally different compounds, and to indicate the structure of each. In the case of pentane, however, three isomers are known, and in that of hexane there are five. In all such cases where there are more than two isomers we must devise other names and these names should be such as to fully express the difference in structure between the isomeric compounds.

Systematic Nomenclature.—That compound which by synthesis or decomposition is shown to have the structure represented by the straight chain formula is always known as the *normal*. In strictly systematic nomenclature this name is often omitted, but implied, so

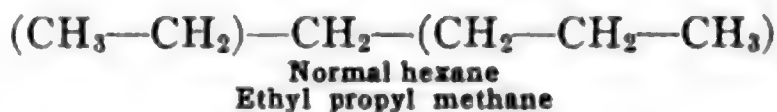
that the simple *unqualified systematic name always means the compound with the normal constitution*. According to what may be called the old system of nomenclature the other isomeric compounds were given names which indicate the radicals linked together to form a compound possessing a definite constitution. The compounds were further considered as *derivatives of methane*. Let us take two of the five isomeric hexanes as an illustration. Normal hexane or simply hexane may be prepared by the action of sodium upon **normal propyl iodide** (p. 29) which proves its constitution to be that of **di-propyl** or **propyl propane**, viz.,



The same hexane, however, may also be prepared from **pentyl iodide** and **methyl iodide** with sodium so that it may be represented as containing the two radicals **normal pentyl** and **methyl**, and could be called **pentyl methane**,



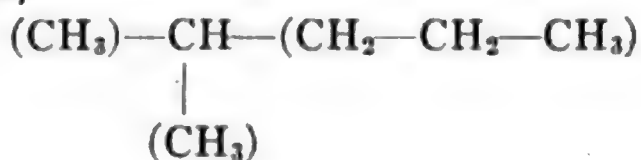
Still another synthesis yields the same hexane by which it may be shown to be represented by the two radicals *ethyl* and *normal propyl*, both substituted in methane as follows:



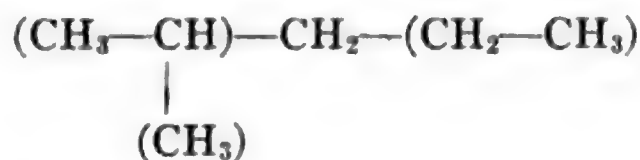
Now each of these groupings of the radicals is based upon definite reactions of synthesis so that they are all correct. Also they all indicate clearly the exact constitution of the compound as only a normal structure can result from the union of either of these sets of radicals. In the case of this hexane of course we need no other name than **normal**, and the others are, therefore, discarded. For the isomeric hexanes, however, we do need other names, but we shall see that in each case there are several names that may be used.

Just as we have shown what names may be applied to normal hexane it may also be shown that the hexane with boiling point of 62° may be synthesized by three sets of reactions which prove that it has the structure represented by the following formula which is identical in the three cases. The names assigned indicate the grouping of the radicals as effected by the different alkyl radicals used in each synthesis. In the formula these radicals are enclosed in parentheses.

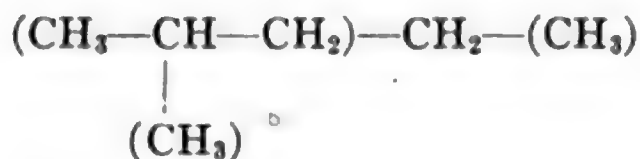
(1) **Di-methyl normal propyl methane,**



(2) **Ethyl iso-propyl methane,**



(3) **Methyl iso-butyl methane,**



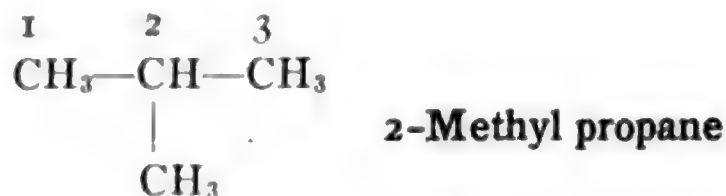
In the same way it may be shown that the other three hexanes may each be given several different names. It must be emphasized that *all of these names* for any one compound indicate the *same structure*. The difference in the names depends simply upon the way in which we divide the group of carbons into smaller groups or radicals, and this depends on definite reactions, each one of which is correct, and each indicates the same structure through a different but correct grouping. We see, therefore, right at the beginning of our study the confusion which may arise by the use of different names for the same compound, and the difficulty of selecting one name as more desirable than the others.

Official Nomenclature.—In order to avoid this confusion a congress of chemists which met in Geneva in 1892 adopted an *Official System of Nomenclature*. The names according to this system and known as the *Official Names* (abbreviated O. N.) are now used in all reference books and dictionaries, such as Beilstein, "Handbuch der Organischen Chemie" and Richter, "Lexikon der Kohlenstoff-Verbindungen." It

would be out of place in a book such as this to explain the entire system or to adopt it absolutely, but enough can be given at this point in connection with the isomeric hydrocarbons to enable the student to grasp some of the fundamental ideas and to understand the official names as they may be given. For many of the simpler compounds considered in this book both the official name and the commonly accepted name will be given, the latter being usually given first. It should be said that in neither of the reference books mentioned nor in any other book, so far as the author knows, is the official system used exclusively or without more or less independent choice. Old and commonly used names are difficult to replace and they will probably always be used. In the case of new compounds, however, the official system is universally adopted.

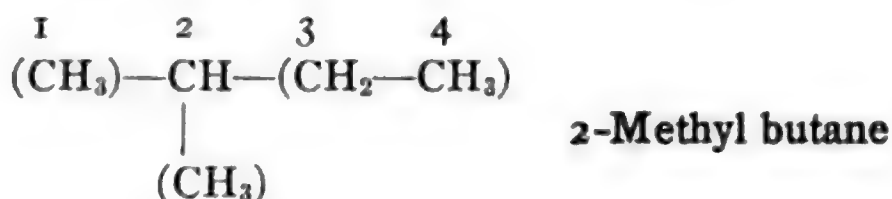
In the official nomenclature, instead of referring compounds to methane as derivatives of it, they are considered as derivatives of *that hydrocarbon corresponding to the longest straight carbon chain which is present in the compound* as represented by the established structural formula. The position of the substituting elements or radicals is indicated by *numbers* or by *Greek letters* applied to the carbons of the straight chain, *i.e.*, the carbons of the root hydrocarbon, *beginning with the end carbon nearest to the substituting radical or element*. The normal compounds simply retain the hydrocarbon name so that the simple names **pentane**, **hexane**, **heptane**, mean in every case the *normal* hydrocarbon. The branched chain or isomeric compounds are, therefore, the only ones which we need to consider now.

Iso-butane has the structure

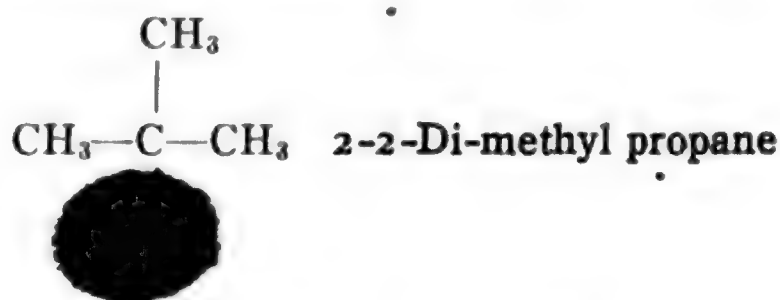


Instead of considering it as a derivative of methane it is considered as a derivative of *propane* because three carbons is the longest straight chain of carbon atoms present, and the three carbon hydrocarbon is propane. It is then *methyl propane* in which the methyl is linked to carbon atom number *two*. Its name is written as follows: **2-methyl propane**.

The pentane which boils at 30° was formerly called **di-methyl ethyl methane** or simply **iso-pentane**, its structure being:

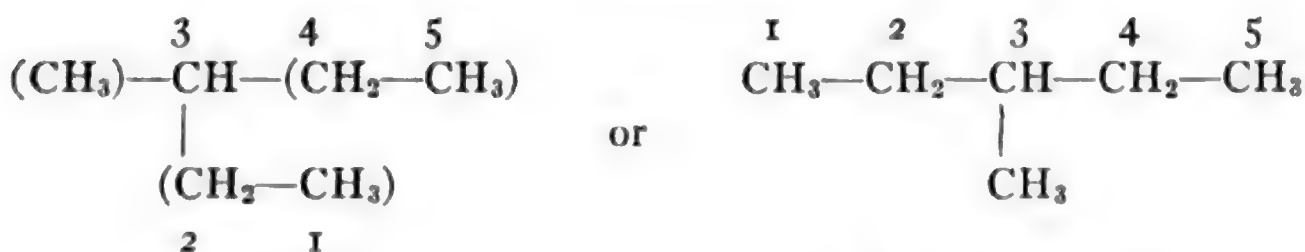


In this formula four carbons is the longest straight chain, and it is, therefore, a **butane** derivative with **methyl** linked to carbon 2. Its official name is **2-methyl butane**. The pentane boiling at 9° is by the old system **tetra-methyl methane**.



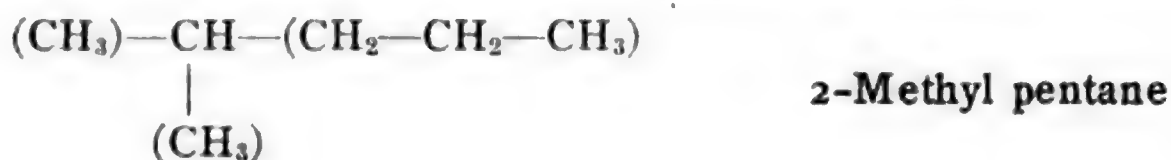
In this compound three carbons constitute the longest unbranched chain and in this *two methyl groups* are linked to carbon atom 2. We write this name **2-2-di-methyl propane**.

The hexane boiling at 64° was called **methyl di-ethyl methane**, as shown in the first formula. If, however, we write this structural formula differently, but representing the *same* structure, we see that the longest unbranched chain consists of *five* carbons.

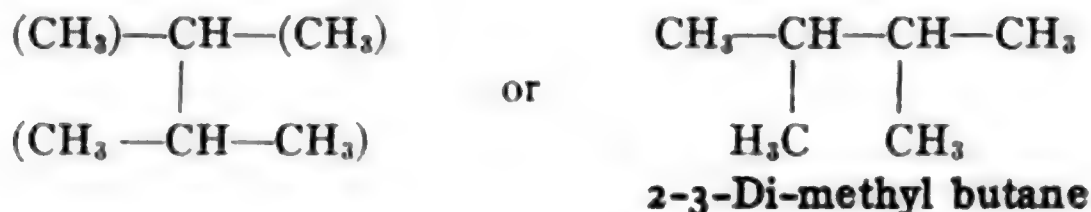


3-Methyl pentane

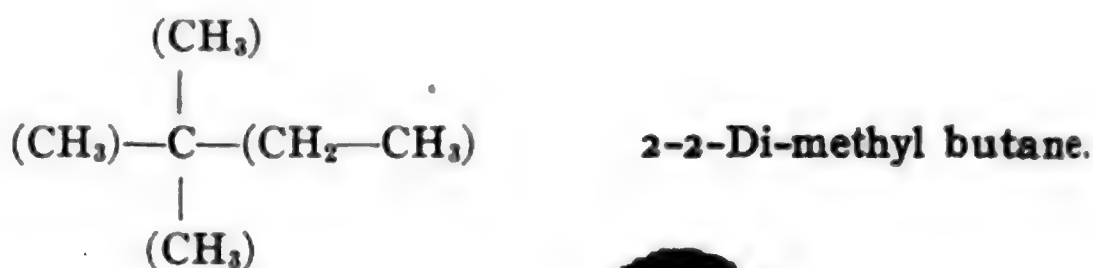
It is then a **pentane** derivative (*i.e.*) **3-methyl pentane**. The hexane boiling at 62° , viz., **di-methyl propyl methane** is **2-methyl pentane**:



The hexane boiling at 58° was **di-methyl iso-propyl methane**. Its official name is **2-3-di-methyl butane**:



The hexane boiling at 48° was **tri-methyl ethyl methane**. It is **2-2-di-methyl butane**:



This may at first seem very confusing, but it is well, if at the beginning the fundamentals of this official nomenclature are mastered. The whole system will then become clearer as we proceed, and the names will become more familiar. It may seem hardly necessary with the relatively small number of compounds which we shall study to use the official names. We must realize, however, that these few compounds constitute only an exceedingly small part of the more than 200,000 known compounds made up, for the most part, of the same four or five elements. An understanding, or more particularly a working knowledge, of books of reference and original literature concerning these compounds can only be gained through familiarity with this system of official nomenclature.

In order to help fix the matter in our mind, and to bring the facts we have been discussing together, the following comparative table may be of value.

TABLE II.—NOMENCLATURE OF THE HYDROCARBONS

Official name	Structural formula	B.P.	Structural formula with old system grouping	Names by old system
Butanes				Butanes
Butane.....	$\text{CH}_3\text{—CH}_2\text{—CH}_2\text{—CH}_3$	+ 1.0°	$\text{CH}_3\text{—CH}_2\text{—CH}_2\text{—CH}_3$	Normal butane
2-Methyl propane.....	$\begin{array}{c} \text{CH}_3\text{—CH—CH}_3 \\ \\ \text{CH}_3 \end{array}$	- 11.5°	$\begin{array}{c} \text{CH}_3\text{—CH—CH}_3 \\ \\ \text{CH}_3 \end{array}$	Tri-methyl methane (Iso-butane)
Pentanes				Pentanes
Pentane.....	$\text{CH}_3\text{—CH}_2\text{—CH}_2\text{—CH}_2\text{—CH}_3$	+ 37.0°	$\text{CH}_3\text{—CH}_2\text{—CH}_2\text{—CH}_2\text{—CH}_3$	Normal pentane
2-Methyl butane.....	$\begin{array}{c} \text{CH}_3\text{—CH—CH}_2\text{—CH}_3 \\ \\ \text{CH}_3 \end{array}$	30.0°	$\begin{array}{c} \text{CH}_3\text{—CH—CH}_2\text{—CH}_3 \\ \\ \text{(CH}_3\text{)} \end{array}$	Di-methyl ethyl methane (Iso-pentane)
2,2-Di-methyl propane..	$\begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_3\text{—C—CH}_3 \\ \\ \text{CH}_3 \end{array}$	9.0°	$\begin{array}{c} \text{(CH}_3\text{)} \\ \\ \text{(CH}_3\text{)—C—(CH}_3\text{)} \\ \\ \text{(CH}_3\text{)} \end{array}$	Tetra-methyl methane
Hexanes				Hexanes
Hexane.....	$\text{CH}_3\text{—CH}_2\text{—CH}_2\text{—CH}_2\text{—CH}_2\text{—CH}_3$	69.0°	$\text{CH}_3\text{—CH}_2\text{—CH}_2\text{—CH}_2\text{—CH}_2\text{—CH}_3$	Normal hexane
3-Methyl pentane.....	$\begin{array}{c} \text{CH}_3\text{—CH}_2\text{—CH—CH}_2\text{—CH}_3 \\ \\ \text{CH}_3 \end{array}$	64.0°	$\begin{array}{c} \text{CH}_3\text{—CH}_2\text{—CH—CH}_2\text{—CH}_3 \\ \\ \text{(CH}_3\text{)} \end{array}$	Methyl di-ethyl methane
2-Methyl pentane.....	$\begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_3\text{—CH—CH}_2\text{—CH}_2\text{—CH}_3 \end{array}$	62.0°	$\begin{array}{c} \text{(CH}_3\text{)} \\ \\ \text{(CH}_3\text{)—CH—CH}_2\text{—CH}_2\text{—CH}_3 \end{array}$	Di-methyl propyl methane
2,3-Di-methyl butane....	$\begin{array}{c} \text{CH}_3 \quad \text{CH}_3 \\ \quad \\ \text{CH}_3\text{—CH—CH—CH}_3 \\ \quad \\ \text{H}_3\text{C} \quad \text{CH}_3 \end{array}$	58.0°	$\begin{array}{c} \text{(CH}_3\text{)} \quad \text{(CH}_3\text{)} \\ \quad \\ \text{(CH}_3\text{)—CH—CH—CH}_3 \\ \quad \\ \text{(H}_3\text{C)} \quad \text{(CH}_3\text{)} \end{array}$	Di-methyl iso-propyl methane
2,2-Di-methyl butane....	$\begin{array}{c} \text{CH}_3 \quad \text{CH}_3 \\ \quad \\ \text{CH}_3\text{—C—CH}_2\text{—CH}_3 \\ \\ \text{CH}_3 \end{array}$	48.0°	$\begin{array}{c} \text{(CH}_3\text{)} \quad \text{(CH}_3\text{)} \\ \quad \\ \text{(CH}_3\text{)—C—CH}_2\text{—CH}_3 \\ \\ \text{(CH}_3\text{)} \end{array}$	Tri-methyl ethyl methane

Higher Hydrocarbons.—It will not be necessary to dwell at any length upon the higher members of the series. The names, formulas, physical constants and the number of isomers known or isolated are given in the table (p. 19). Further facts in regard to any known individual may be obtained by referring to such books as **Beilstein** and **Richter**.

As the number of carbon atoms increases the possibilities of isomerism increase likewise, and very rapidly as shown by the following table:

TABLE III.—ISOMERIC HYDROCARBONS

Hydrocarbon	Number of isomers theoretically possible	Number of known compounds
Butanes, C_4H_{10}	2	2
Pentanes, C_5H_{12}	3	3
Hexanes, C_6H_{14}	5	5
Heptanes, C_7H_{16}	9	5
Octanes, C_8H_{18}	18	2
Nonanes, C_9H_{20}	35	3
Decanes, $C_{10}H_{22}$	75	6
Undecanes, $C_{11}H_{24}$	159	1
Dodecanes, $C_{12}H_{26}$	355	1
Tridecanes, $C_{13}H_{28}$	802	1

The higher members above heptadecane are wax-like solids at ordinary temperatures. They occur naturally in petroleum and ozokerite, and are obtained as mixtures in the higher distillation products of petroleum, viz., in paraffin oil, paraffin and vaseline. They are also obtained as distillation products from coal, wood and fish oil. The separation of individual hydrocarbons by the fractional distillation of these mixtures is a very difficult operation, so that the preparation of the pure hydrocarbons is always accomplished by means of one of the general methods of synthesis from related compounds. These methods are those for preparing the hydrocarbons from the next lower hydrocarbon, discussed on pages 16–29, and those for preparing hydrocarbons from alcohols and unsaturated hydrocarbons which will be discussed when these compounds are considered.

Petroleum

The consideration of petroleum belongs with our study of the hydrocarbons for, though other compounds are present, the greater part are hydrocarbons. The hydrocarbons found in petroleum are not, however, all members of the methane or saturated series which we have been discussing but represent practically every group or series of hydrocarbons some of which we shall study later. Nevertheless it seems better to present the subject at this time in connection with the first series of hydrocarbons inasmuch as the most important facts and problems in connection with petroleum are not those of constitution or of the systematic relationship of the constituents to other organic compounds, but are those of an industrial nature involving largely physical factors.

Occurrence.—The geographical distribution of petroleum in the earth is very wide and only a few large land areas are found to be without it. Africa, the very northern part of North America and the northern part of Siberia are practically without any known deposits. The most abundant fields at present are (1) The United States; Pennsylvania, Ohio, Indiana, Texas and California; (2) Russia; especially in the region of the Caspian Sea, the Baku peninsula; (3) Austria; Galicia; (4) Mexico; (5) Italy, Roumania, Alsace, Burma, Java and Japan. Of these various regions the two largest, viz., the United States and Russia, furnish at present over 90 per cent of the world's supply.

Physical Properties.—Crude petroleum is a more or less dark colored fluorescent liquid with a characteristic odor. The specific gravity usually lies between 0.74 and 0.97 but in a few cases is as high as 1.3.

Chemical Character.—In its chemical character petroleum is not a single compound but is a very complex mixture of a large number of compounds. Its approximate percentage composition is, carbon 87.0 per cent, hydrogen 13.0 per cent, with small and varying amounts of oxygen, sulphur and nitrogen. A more detailed statement of its composition may be given as follows: Carbon, 79.5–88.7 per cent, hydrogen 9.6–14.8 per cent, nitrogen 0.15–1.1 per cent, sulphur 0.06–3.0 per cent and oxygen in traces. There is also a slight ash amounting to about 0.10 per cent which may contain traces of calcium, iron, aluminium, copper, silver, arsenic and phosphorus. The oxygen com-

pounds present are phenols and organic acids usually amounting to less than 1.0 per cent. Nitrogen which is found in Texas petroleum to the amount of 1.0 per cent is usually much less than this and is present as organic bases and ammonia. Sulphur which is usually present in small amounts, 0.1–0.15 per cent is found in the petroleum of Ohio, Indiana, Texas and Virginia in amounts as high as 1.3 per cent and even 3.0 per cent. It is present as mercaptans, thiophene and some other compounds. As the presence of sulphur compounds is very objectionable on account of their odor, and on account of the products of volatilization and combustion, their removal is necessary. This caused much trouble originally in the refining of the oils from these districts.

While all of these various compounds have been found to be present, the predominating constituents are hydrocarbons. The individual hydrocarbons that have been found are very many, probably over one hundred, but they are practically all representatives of three main series and petroleum from different regions are characterized by a predominance of one series over the others. The principal series found are (1) *Hydrocarbons of the Methane or Saturated Series*. The petroleum characterized by these hydrocarbons are those of Pennsylvania, Ohio, Indiana and Galicia. (2) *Hydrocarbons of the Ethylene Unsaturated Series*. These are characteristic of the petroleum of California and Burma. (3) *Hydrocarbons of the Cyclic Series*. The *saturated* cyclic hydrocarbons known as **naphthenes** are characteristic of Russian (Baku) petroleum and are also found in that from Galicia. In some cases also these petroleum contain as much as 10 per cent of unsaturated cyclic hydrocarbons of the **benzene** series. The higher members of the methane series of hydrocarbons, which are present especially in the product known as **paraffin**, are found in very different amounts. American petroleum contains usually about 2.5–3.0 per cent, while the Russian oil contains only about 0.25 per cent. On the other hand, the petroleum of Java, India and some from Roumania contain an exceptionally large amount of these solid hydrocarbons, even as much as 40 per cent, which gives these oils a very high specific gravity.

Distillation Products.—The importance of petroleum as a commercial substance lies in the wide industrial use of the various products obtained from it by distillation. As petroleum is a mixture of gaseous liquid and solid hydrocarbons both it and its distillation products are

combustible substances. The most important use of the products are therefore as sources of heat and light.

Heat of Combustion.—In Table IV there is given in Calories (large) per gram the heat of combustion of petroleum from different regions compared with two of the hydrocarbons and with some other substances.¹

TABLE IV.—HEAT OF COMBUSTION OF PETROLEUM, ETC.

Substance	Calories (large) per gram
Methane.....	13.065
Ethylene.....	11.805
Petroleum, Russian (Balakhany).....	11.700
Petroleum, light, Russian (Baku).....	11.460
Petroleum, heavy, Russian (Baku).....	10.800
Petroleum, heavy, Pennsylvania.....	10.672
Petroleum, light, West Virginia.....	10.223
Petroleum, heavy, West Virginia.....	10.180
Petroleum, light, Pennsylvania.....	9.963
Petroleum, American (average).....	9.771
Petroleum, Alsace.....	9.708
Coal.....	7.500
Coke.....	6.500
Peat.....	4.500
Wood.....	2.800

In the process of distillation the petroleum is subjected to fractionation. The fractions like petroleum itself, are not single compounds but are mixtures of hydrocarbons mainly. The fractions obtained are controlled more or less by the demands of the trade and may thus vary within moderate limits. The fractions are also dependent upon the crude material, *i.e.*, the region from which the petroleum came and also somewhat upon the refinery where the distillation is carried out. Any data that may be given, therefore, in the following tables must be considered in this light and as indicating general facts, approximate limits of boiling point, specific gravity, etc.

¹ The data in Tables IV, V, VI are taken from "*Petroleum and Its Products*," Boverton Redwood, London, 1896, pp. 190, 191, 194, 203.

Light Oils.—The boiling point of petroleum from different regions covers quite a temperature range, viz., from 74° to 135° . When distilled the first large fraction, passing over below 130° or 150° yields products known as light oils. The fraction is again distilled and yields the following oils:

	B.P.
Petroleum ether and rhigoline.....	$40^{\circ}-70^{\circ}$
Gasoline.....	$70^{\circ}-80^{\circ}$
Benzine.....	$80^{\circ}-100^{\circ}$
Ligroine.....	$100^{\circ}-120^{\circ}$
Cleaning oil.....	$120^{\circ}-150^{\circ}$

Illuminating or Burning Oils.—The second large fraction with a range of boiling point between 150° and 300° yields burning oils, the different sub-fractions being used in lamps for illumination. This distillate by further fractionation yields the following products which are differentiated by specific gravity rather than boiling point.

	Sp. Gr.
Kaiser oil.....	.780-.800
Kerosene (American).....	.800-.810
Kerosene (Russian).....	.820-.825
Prime white oil.....	.800-.806
Standard white oil.....	.808-.812
Astraline.....	.850-.860

Lubricating or Heavy Oils.—Oils which distil above 300° are used for lubricating purposes and the different smaller fractions into which this portion of the distillate is divided are used as different grades of lubricating oils.

The following table gives the various smaller fractions usually obtained with the boiling points and specific gravities.

TABLE V.—COMMERCIAL DISTILLATION PRODUCTS OF PETROLEUM
Light Oils, B.P. 40°–150°

	B.P.	Sp. Gr.
Petroleum ether (Rhigoline).....	40°–70°	0.650–0.660
Benzine (U. S.).....	50°–60°	0.670–0.675
Gasoline.....	70°–80°	0.640–0.667
Benzine (English).....	80°–100°	0.667–0.707
Ligroine.....	100°–120°	0.707–0.722
Cleaning oil.....	120°–150°	0.722–0.737

Illuminating Oils, B.P. 150°–300°

Kaiser oil.....	0.780–0.800
Kerosene (American).....	0.800–0.810
Kerosene (Russian).....	0.820–0.825
Prime white oil.....	0.800–0.806
Standard white oil.....	0.808–0.812
Astraline.....	0.850–0.860

Lubricating Oils, B.P. 300°–

Solar oil.....	0.860–0.880
Mixing oil.....	0.880–0.890
Spindle oil I.....	0.895–0.900
Spindle oil II.....	0.900–0.906
Machine oil I.....	0.906–0.910
Machine oil II.....	0.910–0.915
Cylinder oil (bright).....	0.915–0.920
Cylinder oil (dark).....	0.920–0.950
Vulcan oil.....	0.910–0.960

The following table gives the percentage yield as obtained, from different petroleum of (a) light oils, benzine and gasoline; (b) illuminating oils, kerosene; (c) lubricating oils, including solid products and (d) residue, coke.

TABLE VI.—PERCENTAGE YIELD OF COMMERCIAL PRODUCTS FROM DIFFERENT PETROLEUMS

Source of petroleum	Sp. Gr.	Light oils; benzine, gasoline, per cent	Illuminating oils; kerosene, per cent	Lubricating oils and solid prod- ucts, per cent	Coke, per cent
Pennsylvania.....	0.810	20.0	50.0	25.3	1.12
Pennsylvania.....	0.797	21.0	74.1	1.36
Pennsylvania.....	0.787	32.0	64.4
Pennsylvania.....	0.802	21.0	74.3	1.4
Pennsylvania.....	0.788	18.1	71.1	0.8	0.1
Ohio (Macksburg)....	0.829	11.0	49.0	35.7	1.8
Ohio (Lima).....	0.839	83.0	6.9	4.1
Wyoming.....	0.911	2.5	27.5	53.0	11.0
California.....	0.844	12.5	22.0	42.6	10.2
Mexico.....	0.874	37.0	62.2	0.5
Russia.....	0.873	6.3	32.5	57.1	3.0
Russia.....	0.780	48.9	43.9
Russia.....	0.853	20.0	40.0	35.0
Russia.....	0.884	20.0	20.0	50.0	5.9
Galicia.....	0.845	12.5	37.5	40.7	8.3
Alsace.....	0.886	4.0	31.4	52.7	7.9
Zante.....	1.02	76.2	18.4

Benzene, Gasoline.—Two products obtained from petroleum are of especial interest and importance. One of these is the individual hydrocarbon **benzene**, which is obtained in much larger yields from coal tar and is of importance in connection with the manufacture of dyes and explosives. The other is the commercial product known as **gasoline**, which is a mixture of hydrocarbons and is used largely as motive power in gasoline engines for automobiles and air planes. Distinction should be made between **benzene**, which is a single compound and **benzine**, which is a mixed commercial product containing numerous hydrocarbons and which is similar to gasoline and kerosene. (See Part II.) Almost all crude petroleum yields some benzene but in no large amount, while gasoline is one of the light oil fractions always obtained. Because of the value of these two products much attention has been given during recent years to increasing the yield. The study of the temperature and pressure conditions affecting the production of benzene and gasoline has been thoroughly gone into with the result that several processes have been patented. The most important ones are

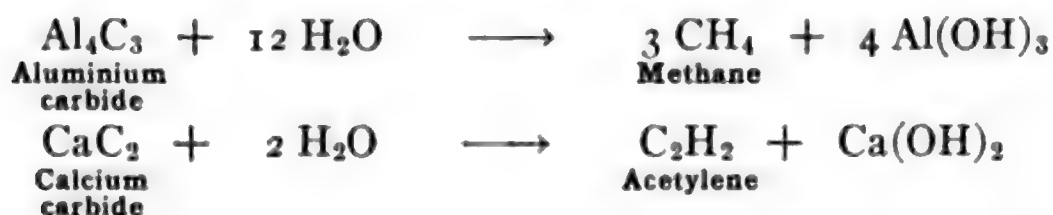
those of the Standard Oil Co., Hall of England and Rittman of the U. S. Bureau of Mines. The principle involved in all of these is known as *cracking*. The petroleum either in the liquid phase or gaseous phase is super-heated under pressure and then allowed to expand and distil. By these processes the yield of both benzene and gasoline has been materially increased so that a larger per cent of these products is obtained at the expense of either other light oil constituents or at the expense of the illuminating oil fraction.

Vaseline and Paraffin.—Two solid products obtained from petroleum are the common pharmaceutical substance **vaseline**, a hydrocarbon mixture melting at about 35° and the white solid known as **paraffin**, also a hydrocarbon mixture melting at about 40° – 60° . The properties and uses of these two substances are too common to require any further description.

Tar and Coke.—The **tar** residue obtained from petroleum is used for various purposes such as water-proofing, wood-preserving, road-making, etc., in a similar way to the tar obtained from coal distillation. The coke obtained as the final solid residue is used as fuel.

Origin of Petroleum.—The theories as to the origin of petroleum are of three kinds, (a) *animal origin*, (b) *vegetable origin*, (c) *inorganic origin*. (a) The first theory that petroleum is of animal origin assumes that it originated from the geologic decomposition of sea animals. In such a decomposition most of the nitrogen of the animal protein would be lost but there would naturally be some left in the petroleum. That most petroleums contain only traces of nitrogen has been considered as an objection to the theory of animal origin but the finding of Texas petroleum with as much as 1.0 per cent of nitrogen gives support to the theory. The theory has been advocated especially by **Engler** and **Holde**. The former, by the distillation of fish oil under pressure, showed that animal fats may be converted into hydrocarbons with the formation of products analogous to crude petroleum. (b) The theory of vegetable origin is supported by the similarity of the compounds found in petroleum with the products obtained by the distillation of such vegetable substances as wood, peat or coal. It is opposed, however, by the fact that petroleum deposits are not found in the strata of the earth which contain plant remains. (c) The theory of the inorganic origin of petroleum has been held by such men as **von Humboldt**, **Mendelejeff**, and more recently by **Moissan**. The latter has

shown that numerous metallic compounds of carbon known as *carbides* may be prepared by means of the electric furnace and that these carbides, by the action of water, decompose yielding various hydrocarbons both saturated and unsaturated. The latter by the action of hydrogen in the presence of a catalyser yield saturated compounds.



Further details in connection with the geologic origin and occurrence of petroleum may be obtained from special books on the subject.

II. MONO-SUBSTITUTION PRODUCTS OF SATURATED HYDROCARBONS

(A) MONO-HALOGEN SUBSTITUTION PRODUCTS

ALKYL HALIDES $R-X$ HALOGEN ALKANES

The alkyl halides, as has been previously stated, are compounds containing an alkyl radical joined to a halogen element, *i.e.*, **iodine**, **bromine**, **chlorine** or **fluorine**. They are mono-halogen substitution products of the paraffin hydrocarbons. The general facts in regard to them have been so fully discussed, in connection with their relation to the ideas of substitution and isomerism and to the synthetic building up of the hydrocarbons, that there is little to add except to mention the more important individual compounds, and to give their occurrence and uses. The following table gives the chlorides, bromides and iodides of the first four hydrocarbons with their boiling points and specific gravities.

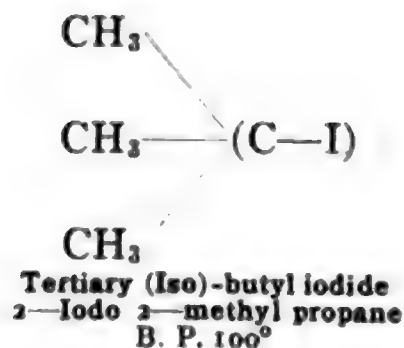
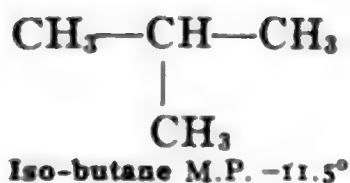
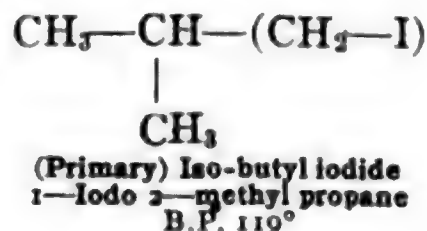
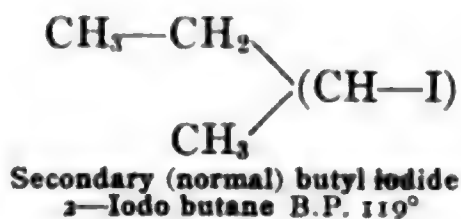
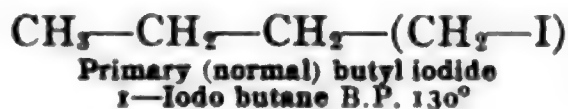
The homologous character of this series may be seen by examination of the table. The boiling points *rise* as we go up the series just as they did in the case of the hydrocarbons. The lowest is **methyl chloride** with boiling point -23.7° , the highest, **butyl iodide**, b. p. 130° . Also the boiling points of the members of each isomeric group *decreases*, *e.g.*, **primary normal butyl iodide** is 130° and **tertiary butyl iodide** is 100° . It will be seen also that there is a similar *rise* in the boiling points from the chlorides to the bromides and then to the iodides giving us a double homologous relationship. The specific gravities become *lower* as we go up the series which is the reverse of the same property in the homologous series of hydrocarbons. This lowering becomes more rapid within the isomeric groups. As we go from the chlorides to the bromides and iodides, however, we find that the specific gravity *increases*.

Isomerism of Alkyl Halides.—In discussing the question of isomerism in connection with the butanes and pentanes (pp. 21-29) we found that, while the two isomeric butanes really yield *four* methyl substitution products, *i.e.*, pentanes, two of them possess the same

TABLE VII.—ALKYL HALIDES

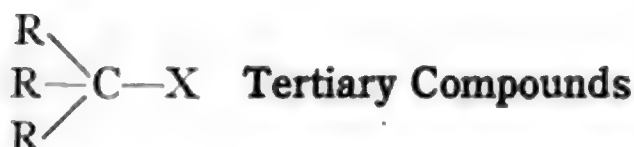
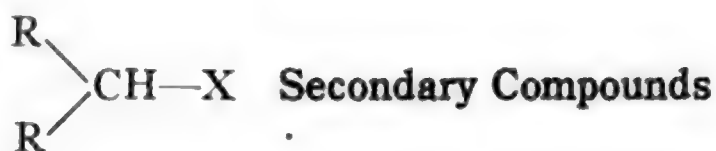
Alkyl radical	Formula (X = halogen)	Chloride		Bromide		Iodide	
		B.P.	Sp. Gr.	B.P.	Sp. Gr.	B.P.	Sp. Gr.
Methyl.....	CH ₃ —X	-23.7°	0.952 (0°)	4.5°	1.73 (0°)	42.8°	2.29 (18°)
Ethyl.....	C ₂ H ₅ —X	+12.2°	0.918 (18°)	38.4°	1.47 (13°)	72.0°	1.94 (14°)
Propyl.....	C ₃ H ₇ —X						
Normal.....	46.5°	0.912 (0°)	71.0°	1.38 (0°)	102.5°	1.78 (0°)
Iso.....	36.5°	0.882 (0°)	60.0°	1.34 (0°)	89.0°	1.74 (0°)
Butyl.....	C ₄ H ₉ —X						
Primary butyl.....	78.0°	0.907 (0°)	101.0°	1.30 (0°)	130.0°	1.64 (0°)
1-Halogen butane	CH ₃ —CH ₂ —CH ₂ —CH ₂ —X						
Secondary butyl.....	68.5°	0.895 (0°)	92.0°	1.20 (10°)	119.0°	1.64 (0°)
2-Halogen butane	CH ₃ —CH ₂ —CH—CH ₃ X						
Iso-butyl.....						
1-Halogen 2-methyl propane	CH ₃ —CH—CH ₂ —CH ₃ CH ₃					119.0°	1.63 (0°)
Tertiary butyl.....						
2-Halogen 2-methyl propane	X—C(CH ₃) ₃	55.0°	0.866 (0°)	72.0°	1.21 (20°)	100.0°	1.57 (0°)

structure so that only *three* are possible which agrees with the facts, as *three* and only three are known. When, however, we substitute iodine in the two isomeric butanes we find that *four* butyl iodides are possible, all of which are different and all of which are known. This will be seen from the following scheme of relationships.



Primary, Secondary and Tertiary Compounds.—The naming of these four isomeric butyl iodides brings us to the consideration of a new point in the nomenclature of organic compounds. In the first compound, which has the straight chain structure, *i.e.*, a *normal* compound, the carbon atom in the group containing the halogen, *viz.*, (CH_2I) is linked to *one other carbon atom*. The same condition is found in the third compound where the structure is that of an *iso* or branched chain. In the second compound, however, which is also *normal*, the

carbon atom which holds the halogen is linked to *two other carbon atoms* and in the fourth compound, which is not normal but contains a branched chain, the carbon atom which holds the halogen is linked to *three other carbon atoms*. These three different groupings, because they are characterized by a carbon atom which is linked to *one, two or three* other carbon atoms, are known as *primary, secondary and tertiary*, and compounds containing such groups are known as primary, secondary or tertiary compounds. Denoting by *R* any radical of one or more carbon atoms, and by *X* any substituting element or group, we have the three kinds of compounds represented by general formulas as follows:



We shall find these three classes of compounds of special importance when we study the alcohols in the next chapter. The names of the first, second and fourth isomeric butyl iodides, as given in the table are, **primary butyl iodide, secondary butyl iodide and tertiary butyl iodide**. As the first two are both straight chain compounds, and the fourth is a branched chain compound the full names include also the terms *normal* or *iso*. The third butyl iodide is also primary, but it is not normal, therefore it is **(primary) iso-butyl iodide**. Thus all substitution products possess two different characters depending upon their structural or constitutional formulas. One of these characters depends upon the nature of the chain of carbon atoms present; if it is a *straight chain* it is a *normal* compound, but if it is a *branched chain* it is an *iso* compound. The other character depends upon the *number of hydrogens and of alkyl radicals joined to the carbon to which the substituting group is linked*. If this carbon has two hydrogens and *one alkyl radical* joined to it, viz., $R-CH_2-X$, it is known as *primary*. If it has

only one hydrogen and *two radicals*, viz., $\begin{array}{c} \text{R} \\ \diagdown \\ \text{CH-X} \\ \diagup \\ \text{R} \end{array}$ it is *secondary*,

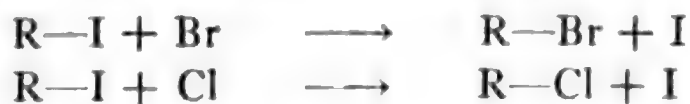
while if it has no hydrogens and *three radicals*, viz., $\begin{array}{c} \text{R} \\ \diagdown \\ \text{R-C-X} \\ \diagup \\ \text{R} \end{array}$ it is

tertiary. Both of these characters are always present in any substitution product. ✓

Official Names of Alkyl Halides.—The official names of the alkyl halides are derived in exactly the same way as in the case of the hydrocarbons. The number of the carbon to which the halogen is joined, together with the name of the halogen, is used as a prefix to the official name of the hydrocarbon in which the halogen is substituted. These names are shown both in the table and in the scheme just given.

Preparation of Alkyl Halides.—We have spoken of the formation of the alkyl halides by the direct action of the halogen upon the saturated hydrocarbon. In the case of chlorine this action takes place at ordinary temperatures as in the reaction between methane and chlorine in the sunlight. Bromine, however, does not act directly at ordinary temperatures but by heating in a sealed tube. Iodine does not act directly with the hydrocarbons. In any case the result is a mixture of several substitution products, and the method is not, therefore, of practical value. Where direct action does not occur the presence of iodine chloride or antimony chloride, which act as carriers, is necessary. The two reactions of most importance in the preparation of these compounds are those involving either alcohols or unsaturated hydrocarbons. These will be taken up when these compounds are studied.

As in some inorganic compounds chlorine replaces bromine or iodine and bromine replaces iodine, so in these alkyl halides the chlorides may sometimes be prepared by replacing bromine or iodine with chlorine, and the bromide from the iodide by means of bromine



Alkyl Halides as Synthetic Reagents.—The general reactions of the alkyl halides are such as result in the replacement of the halogen

by another radical or group. In the **Wurtz** and **Frankland** reactions for the synthesis of saturated hydrocarbons (p. 16), two alkyl radicals become united.

Alkyl halide, $R-(I + Na_2 + I)-R \longrightarrow R-R + 2NaI$ **Hydrocarbon**

Reacting with water, (H—OH), potassium hydroxide, K—OH, or silver hydroxide, Ag—OH, the radical will become united to the *hydroxyl* group, (OH).

Alkyl halide, $R-(X + H)-OH \longrightarrow R-OH + H-X$ **Alkyl hydroxide**

Alkyl halide, $R-(X + Ag)-OH \longrightarrow R-OH + Ag-X$ **Alkyl hydroxide**

Similarly with potassium cyanide, K—CN, and silver nitrite, Ag—NO₂, compounds are obtained in which the radical is united to the *cyanide*, or to the *nitro* group.

Alkyl halide, $R-(X + K)-CN \longrightarrow R-CN + K-X$ **Alkyl cyanide**

Alkyl halide, $R-(X + Ag)-NO_2 \longrightarrow R-NO_2 + Ag-X$ **Nitro compound**

With ammonia the *ammonia residue* (—NH₂) becomes united to the radical,

Alkyl halide, $R-(X + H)-NH_2 \longrightarrow R-NH_2 + H-X$ **Alkyl amine.**

With nascent hydrogen the alkyl halides reform the *hydrocarbon* of the alkyl radical.

Methyl chloride, $CH_3-Cl + H_2 \longrightarrow CH_4 + HCl$ **Methane.**

The alkyl halides are therefore known as *alkylating reagents*, i.e. they are used to introduce an alkyl radical. In this use they are among the most important reagents in organic chemistry and are employed in many technical processes.

In their inorganic compounds the three halogens chlorine, bromine and iodine are in this order in regard to their affinity for other elements. This seems to hold also in their organic compounds as shown by the replacement of iodine by bromine or chlorine, as given previously, and by the fact that alkyl iodides are the *least stable* or the *most reactive*, while the chlorides are the *most stable* or the *least reactive*. This is illustrated by their action upon silver nitrate. Ethyl iodide acts with silver nitrate in alcoholic solution precipitating silver iodide even in the cold.

Ethyl bromide precipitates the silver as bromide only on warming, while ethyl chloride does not react with an alcoholic solution of silver nitrate at all. It should be emphasized in this connection that this reaction of alkyl halides and silver nitrate in alcoholic solution, though probably of the same nature as that in the case of metallic halides and silver nitrate in water solution, is noticeably different in degree. This is accounted for by the fact that in water both metallic halides and silver nitrate are highly dissociated into ions, whereas in alcohol the alkyl halides and silver nitrate are only very slightly dissociated. As alkylating reagents the iodide is the most important because of its greater activity.

Properties and Uses of Alkyl Halides.—The alkyl halides of the lower hydrocarbons are gases or volatile liquids, some of them possessing anesthetic properties making them valuable in medicine. They have a sweet taste, are insoluble in water, but soluble in alcohol and ether.

Methyl Chloride, Chlor-methane, CH_3Cl , is a gas, boiling at -237° . It may be compressed in cylinders in which form it is used as a methylating reagent in the manufacture of dyes. It is also used for producing low temperatures and as a local anesthetic.

Methyl iodide, Iodo methane, CH_3I , is a volatile liquid, boiling at 42.8° . Methyl iodide, **ethyl iodide** and **ethyl bromide** are the most important of the alkyl halide reagents.

Ethyl chloride, Chlor-ethane, $\text{CH}_3\text{—CH}_2\text{Cl}$, and **ethyl bromide, brom ethane, $\text{CH}_3\text{—CH}_2\text{Br}$,** are both used as local anesthetics, the latter in dentistry. The former is a gas, boiling as 12.2° , which can be readily condensed to a liquid and is used technically in this form. Ethyl bromide is a chloroform-like liquid boiling at 38.4° .

Ethyl iodide,	Iodo ethane,	$\text{CH}_3\text{—CH}_2\text{I}$
Propyl iodide,	1-Iodo propane,	$\text{CH}_3\text{—CH}_2\text{—CH}_2\text{—I}$
Iso-propyl iodide,	2-Iodo propane,	$\text{CH}_3\text{—CHI—CH}_3$

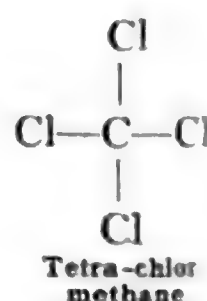
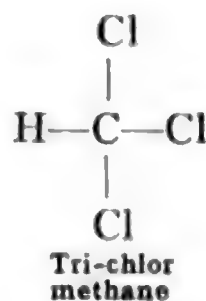
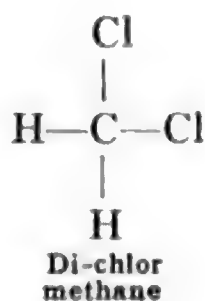
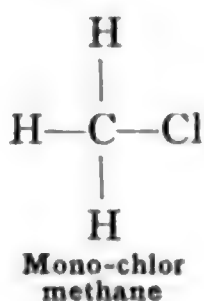
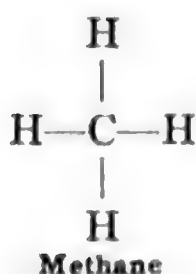
POLY-HALOGEN COMPOUNDS

We have said that substitution is the replacement of *one or more* of the hydrogen atoms, in a hydrocarbon or a hydrocarbon radical, by an equivalent number of other elements or groups of elements. When one monovalent element or group is substituted for one hydrogen, we have

called the compounds *mono-substitution products*. If two hydrogens are similarly substituted we term the resulting compounds *di-substitution products*. When three are substituted we obtain *tri-substitution products*, etc. The general name for substitution products containing more than one substituting group is, *poly-substitution products*.

While it is advisable to consider the different groups of *mono-substitution products* first and by themselves, it is necessary to discuss briefly at this time a few facts in regard to the poly-halogen substitution products in order that we may understand a case of isomerism which is essential in establishing the constitution of **aldehydes** and of **unsaturated hydrocarbons**, both of which are to be studied before we take up in detail the full discussion of poly-substitution products. As we may substitute more than one monovalent element or group for an equal number of hydrogen atoms these substituting elements or groups may be the same or may be different. We shall thus have compounds that will be of mixed character. Also a di-valent element, *e.g.*, oxygen, may be substituted for two hydrogen atoms, etc. For our present purpose, however, we shall confine ourselves to those compounds formed from the first two hydrocarbons, viz., methane and ethane, by the substitution of more than one halogen element of the same kind.

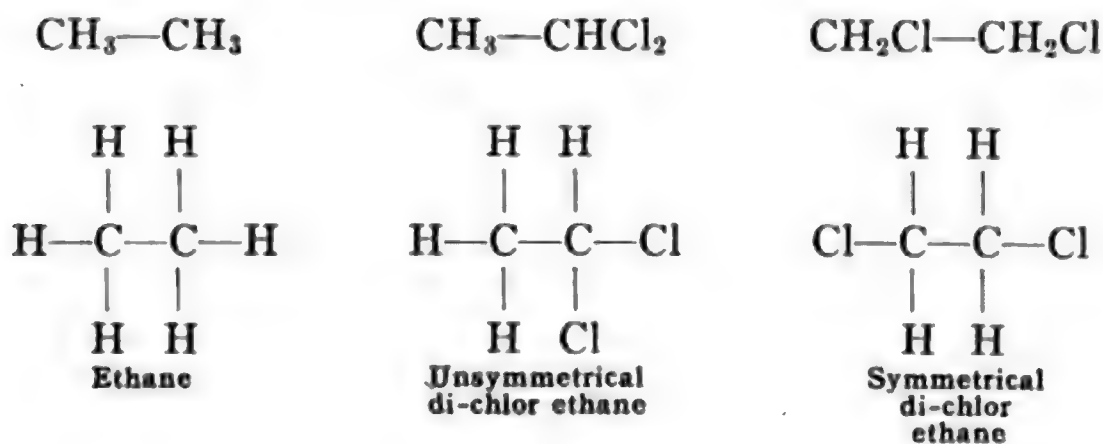
Poly-halogen Methanes.—When methane is acted upon by chlorine or bromine directly a mixture of products is obtained resulting from the substitution of one, two, three or four chlorine or bromine atoms for an equal number of hydrogen atoms. The usual method of preparing these compounds is not by this direct substitution but from other compounds than the hydrocarbons themselves; this will be considered later when we study the compounds in detail. The four chlorine substitution products of methane which are typical of all of the halogen methanes have the formulas, CH_3Cl , CH_2Cl_2 , CHCl_3 and CCl_4 , and in accordance with our ideas of the structure of methane, their constitutional formulas are,



Only *one* each of these compounds, or of the other corresponding halogen compounds, has ever been prepared which has given us our idea of the symmetry of the methane molecule in that all of the hydrogen atoms in methane must be exactly alike so that it makes no difference which one, which two or which three are substituted.

Poly-halogen Ethanes.—Just as we may substitute more than one halogen in methane so, also, there are compounds known in which more than one halogen has been substituted in ethane. The chlorine compounds have the formulas: C_2H_5Cl , $C_2H_4Cl_2$, $C_2H_3Cl_3$, $C_2H_2Cl_4$, C_2HCl_5 , C_2Cl_6 , and are known respectively as **mono-**, **di-**, **tri-**, **tetra-**, **penta-**, and **hexa-chlor ethane**.

Isomerism of Di-chlor Ethanes.—When, however, we study the constitution of the **poly-halogen ethanes** we find that isomerism occurs just as in the case of the propyl iodides and of the hydrocarbons above propane. In the case of ethane it is a fact that only *one* mono-substitution product of any type is known, thereby proving the symmetry of the ethane molecule and the like character of all six of the hydrogen atoms. When *two* hydrogen atoms are substituted by two chlorine atoms *two different* compounds are produced both having the composition $C_2H_4Cl_2$. From the constitution of the ethane molecule, that has been established by its synthesis from methane (p. 16), we can readily see how this may be explained as we may have two hydrogen atoms replaced by two chlorine atoms in two different ways, as follows:



The fact that two compounds exist of the formula ($C_2H_4Cl_2$) means that these two structural formulas must represent different substances. Our ideas and the facts are thus in agreement. Although all six of the hydrogens are alike, and it makes no difference which *one* of the six is substituted by chlorine, as proven by the existence of *only one* mono-

chlor ethane, yet when we replace *two* hydrogen atoms in ethane by *two* chlorine atoms, *two* compounds are possible; as in one case both chlorine atoms are linked to the *same carbon* atom, while in the other they are each linked to a *different carbon* atom. One of the compounds, $\text{CH}_2\text{Cl}-\text{CH}_2\text{Cl}$, is termed **symmetrical di-chlor ethane**, the other $\text{CH}_3-\text{CHCl}_2$, **unsymmetrical di-chlor ethane**. This isomerism of the symmetrical and unsymmetrical di-substitution products of ethane is the important fact to be remembered later on.

(B) MONO-AMINO SUBSTITUTION PRODUCTS

ALKYL AMINES $\text{R}-\text{NH}_2$ AMINO ALKANES

Synthesis.—We have shown that the alkyl halides are mono-substitution products of the hydrocarbons, *i.e.*, one hydrogen of the hydrocarbon has been substituted by a halogen, *e.g.*, methyl iodide, CH_3-I . Now when methyl iodide is treated with ammonia a new compound is formed having the composition CH_5N and the other product of the reaction is hydrogen iodide.

Amines.—This compound and similar ones derived from other hydrocarbons are known as **amines**, and were first discovered by **Wurtz** in 1848. **Hofmann**, in 1850, showed conclusively that these nitrogen containing compounds are to be considered as derivatives of ammonia in which the monovalent nitrogen radical ($-\text{NH}_2$), a residue of ammonia, is linked to an alkyl radical. Methyl iodide is made up of the methyl radical linked to iodine and in the above reaction the iodine leaves the methyl and unites with one hydrogen from the ammonia, the place of the iodine being taken by the residue of the ammonia ($-\text{NH}_2$). The reaction becomes then:

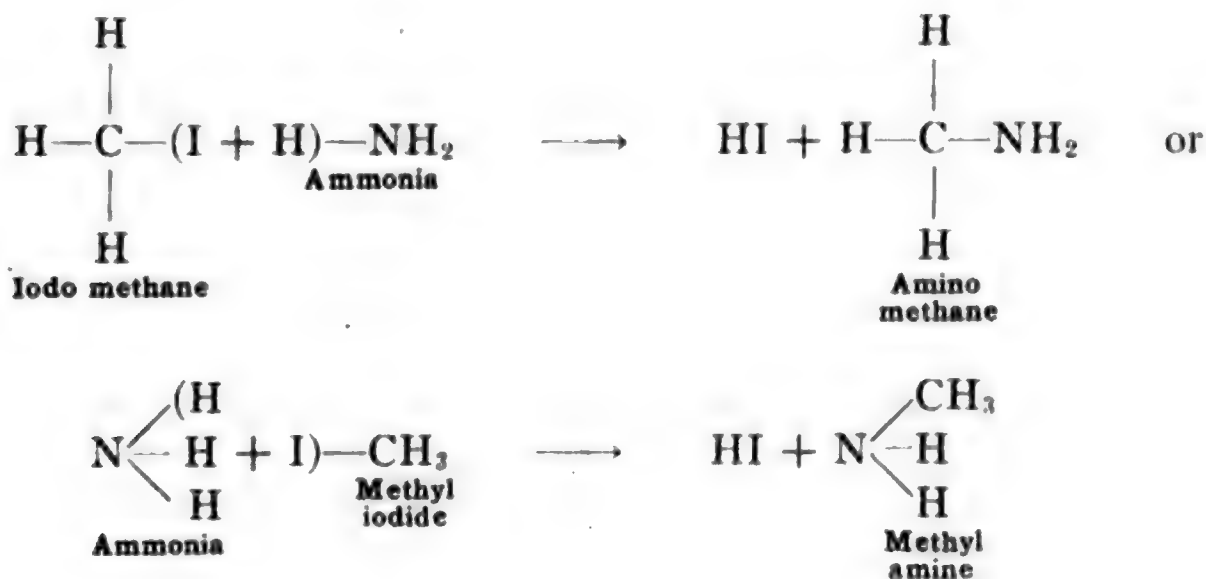


As it is derived from ammonia the group ($-\text{NH}_2$), is given the name of the amino radical. It has never been isolated, and we do not know it as a free substance nor, as has been stated, do we know the radical (CH_3-) as a free substance.

Amino Compounds.—We have previously explained how **mono-chlor methane**, *i.e.*, methane in which one hydrogen atom has been substituted by a chlorine atom, may with equal justice be considered

as **methyl chloride**, *i.e.*, hydrogen chloride in which the hydrogen atom has been substituted by the methyl radical.

In the same way we may consider these new compounds either as *amino substitution products of the hydrocarbons* or as *alkyl substitution products of ammonia*.



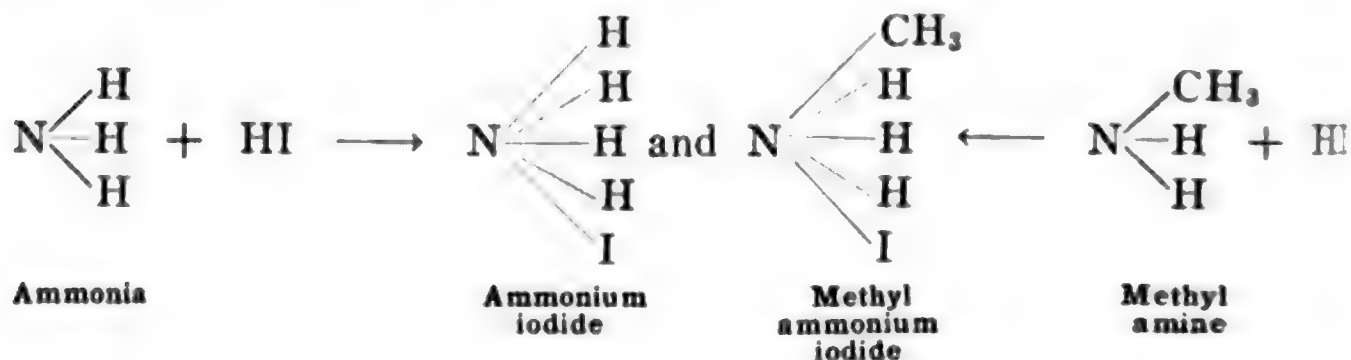
If we consider them as substituted hydrocarbons they are known as *amino* or *amido* substitution products, *e.g.*, **amino methane**. If they are considered as ammonia in which the alkyl group has been substituted, they are called substituted ammonias or **amines**, *e.g.*, **methyl amine**.

Basic Character.—The alkyl amines then are analogous to alkyl halides, and we find a corresponding homologous series, *e.g.*, **methyl amine**, **ethyl amine**, **propyl amine**, etc. They are strongly *basic* compounds, in fact, they are of especial interest because they are more strongly basic than the ammonia from which they are derived.

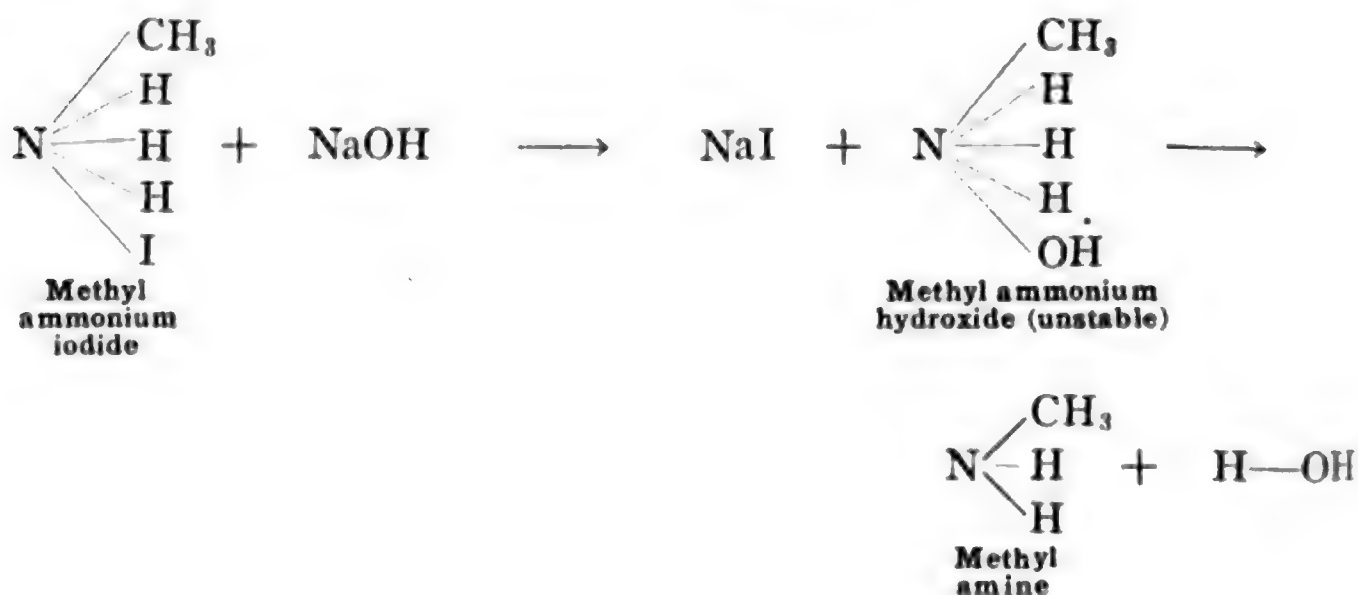
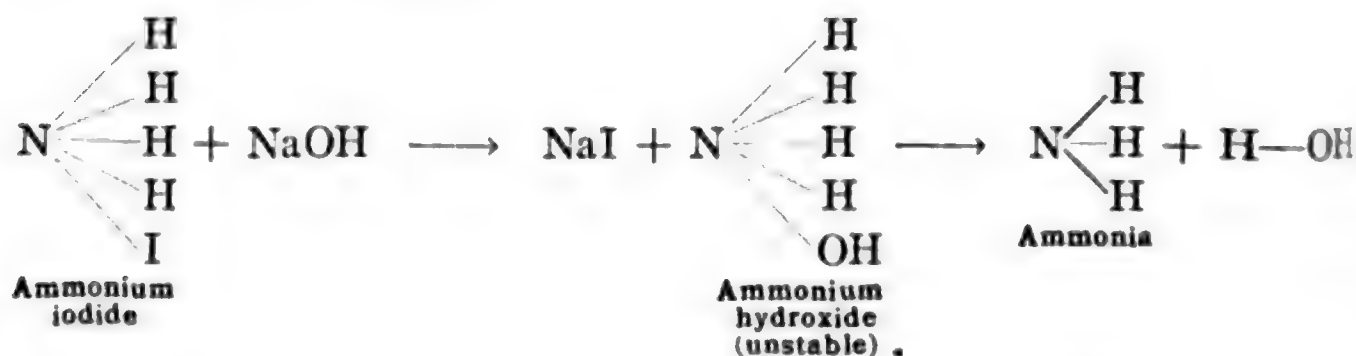
The characteristic properties and reactions of ammonia are also true of the amines. They have a strong fishy, ammonia-like odor, but unlike ammonia the lower ones are inflammable. It was this fact which led to their discovery. Wurtz supposed that the volatile substance he had obtained was ammonia until a flame was accidentally brought near it when it ignited. They are readily soluble in water, and their solutions are alkaline to litmus.

Salts.—When ammonia reacts with an acid, *e.g.*, hydrochloric or hydriodic acid, there is formed an addition product or salt in which the *trivalent nitrogen of ammonia* is converted into the *pentavalent nitrogen*

of the ammonium salt. In the same way when methyl amine reacts with hydriodic acid a salt of the amine is obtained.

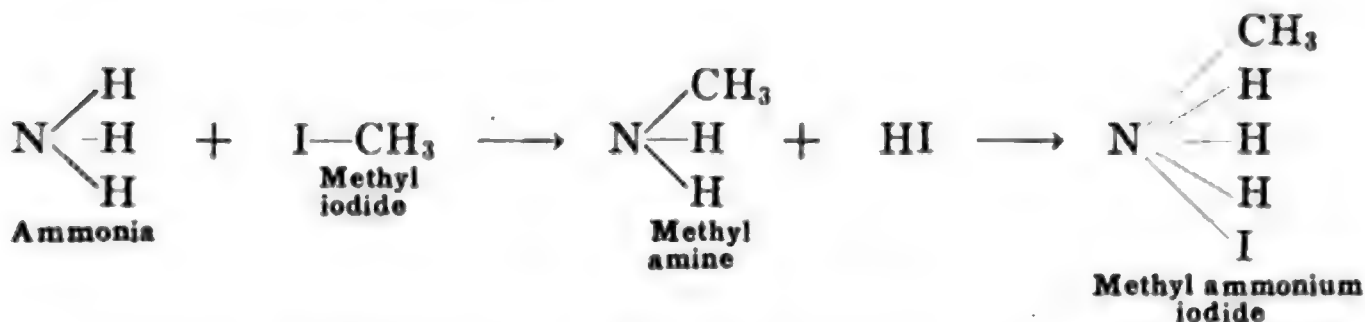


The compound formed from the amine is a substituted ammonium salt viz., **methyl ammonium iodide**. It is known more generally, however, as **methyl amine hydriodide**, and is usually written, $\text{CH}_3\text{—NH}_2\text{—HI}$. When this salt is treated with a stronger base, *e.g.*, sodium hydroxide, the amine is again formed just as ammonia, NH_3 , is set free from its salts by the same reagent.

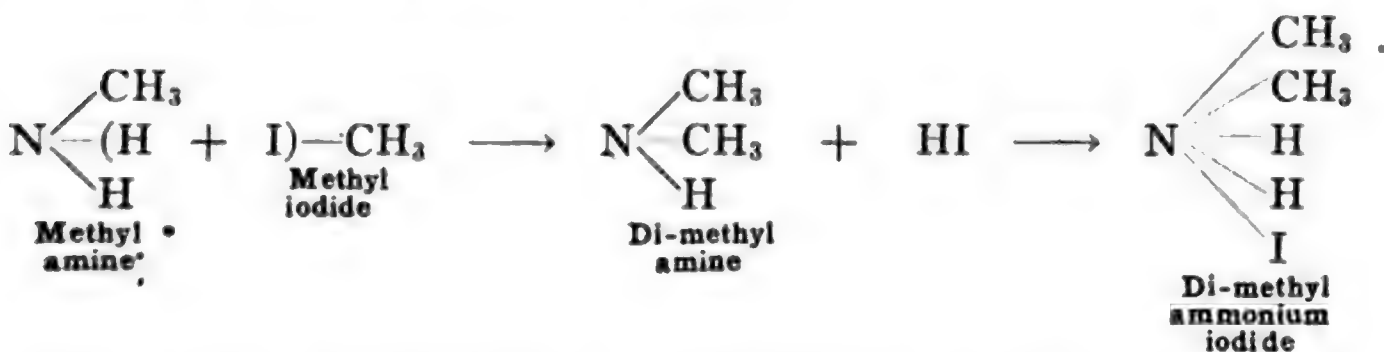


In the reaction previously given for the synthesis of the amines from the alkyl halides the salts of the amines are, in fact, formed as the

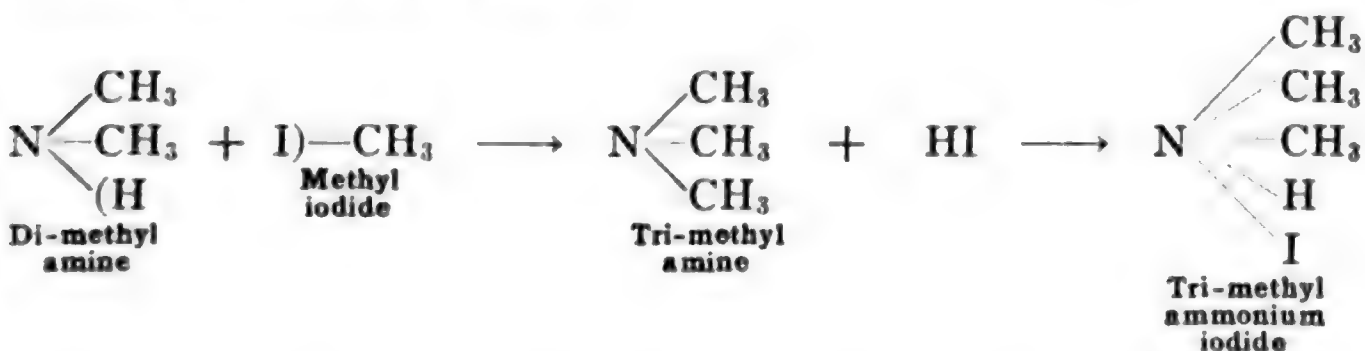
result of a secondary reaction between the amine and the halogen acid, the complete reaction being



Primary, Secondary and Tertiary Amines.—The amines that we have considered, which are formed from ammonia by the replacement of *one* hydrogen by *one* alkyl radical, are termed *primary amines*. They not only act like ammonia in the ways just mentioned, but they *react with alkyl halides* just as ammonia itself does and a *second* hydrogen united to nitrogen is replaced by methyl.

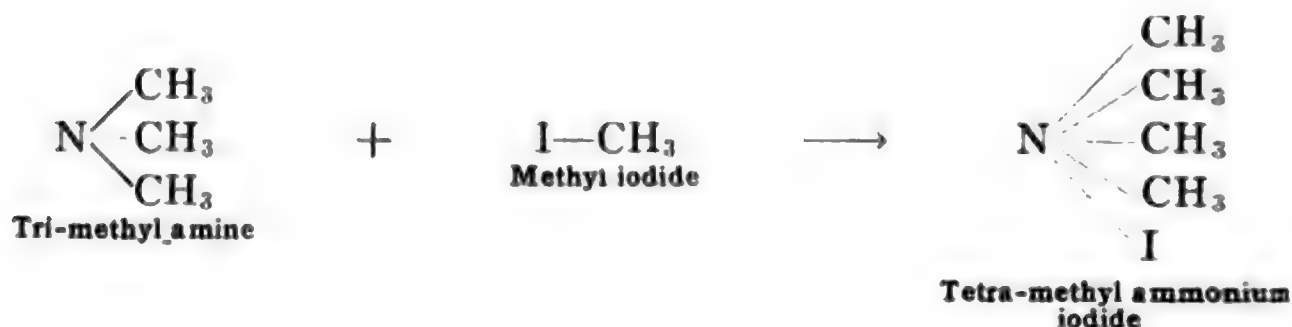


Such an amine resulting from the replacement of *two* of the ammonia hydrogens by *two* methyl or other hydrocarbon radicals is known as a *di-amine* or a *secondary amine*. These di-amines likewise react with alkyl halides in the same way and the *third* ammonia hydrogen is replaced by a radical as follows:



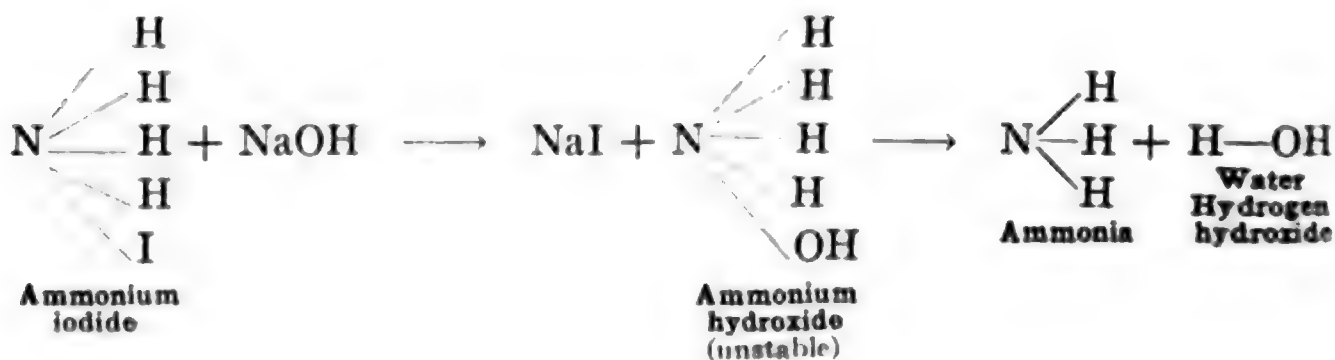
An amine thus related to ammonia in that all *three* of the ammonia hydrogens are replaced by hydrocarbon radicals is called a *tri-amine* or a *tertiary amine*.

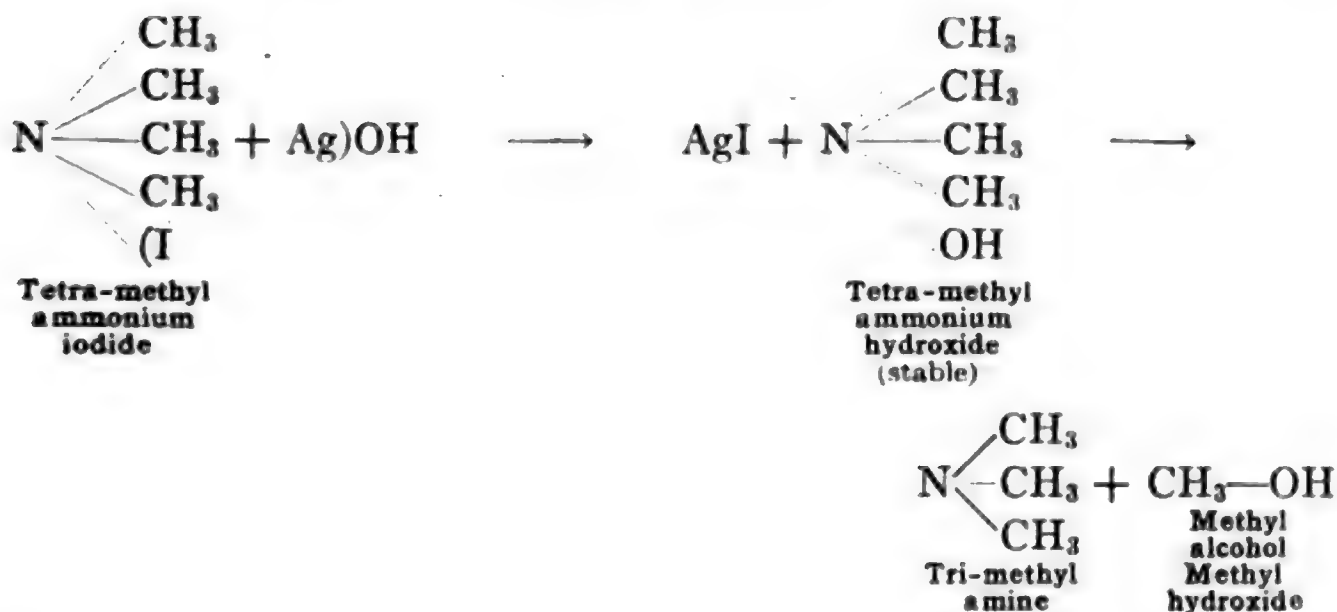
Tetra-methyl Ammonium Salts.—Not only do these tri-amines unite directly with the hydrogen halides forming ammonium salts as above, but, being much *more strongly basic* than the mono- or di-amines, they unite also with the alkyl halides themselves forming salts of similar character. Thus:



These salts are known as *tetra-methyl ammonium salts* or *quaternary compounds*.

When the methyl ammonium salts of the hydrogen halogen acids are decomposed by sodium hydroxide there is probably first formed an ammonium hydroxide-like compound just as in the case of ammonium salts themselves. These hydroxide compounds, like ammonium hydroxide, are not possible of isolation, but decompose as was represented in the reaction as just given for setting free the methyl amine from its hydriodide salt. With the tetra-methyl ammonium salts, however, sodium hydroxide does not set free the tri-methyl amine, and if we use silver hydroxide (moist silver oxide) instead of sodium hydroxide, silver iodide is formed and the *hydroxide of the tetra-methyl ammonium salt* is set free. By heating, this decomposes, **methyl alcohol** being one of the products and **tri-methyl amine** the other. All of the products are thus the methyl analogues of ammonia compounds and water. Writing the two sets of reactions together makes this plain.



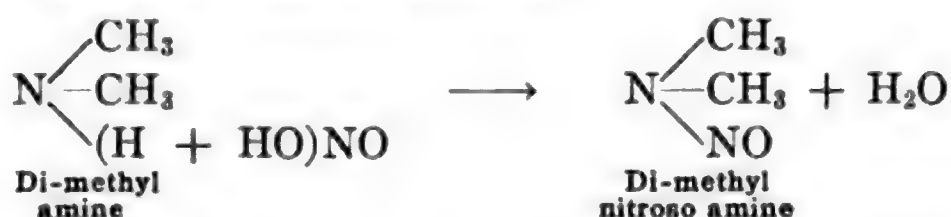


The salts of the amines and halogen acids are all crystalline compounds soluble in water and similar to ammonium salts in every respect. The only hydroxide compound which can be isolated is the tetra-methyl ammonium compound which is stable at ordinary temperatures and decomposes only on heating. The reason for this is undoubtedly in the fact that all of the other hydroxides, those formed from the primary, secondary and tertiary amine salts, have at least *one hydrogen* left in union with the nitrogen, and this hydrogen always breaks off with the hydroxyl forming water, and the amine is left free. In the tetra-methyl ammonium hydroxide there is *no hydrogen* left united to the nitrogen and, therefore, water cannot split off. **Tetra-methyl ammonium hydroxide** is a crystalline substance possessing strong basic, even caustic, properties and absorbs water and carbon dioxide readily from the air. The fact that this compound exists as a stable compound gives support to the belief that the corresponding hydrogen compound, viz., **ammonium hydroxide**, which is so unstable that it does not exist under ordinary conditions, is nevertheless a definite compound possible of existence under conditions which have not been attained.

Distinction Between Primary, Secondary and Tertiary Amines. When an alkyl halide and ammonia react the reaction is not a clean cut one by which either a primary, a secondary, a tertiary or a quaternary amine or amine salt is formed. By regulating the conditions of the reaction the product may have one of these in the greatest amount, but it always contains a mixture of all of the salts. The separation of the amines from each other or the distinguishing of one from the others is, therefore, important. As one of the reactions on which such a sepa-

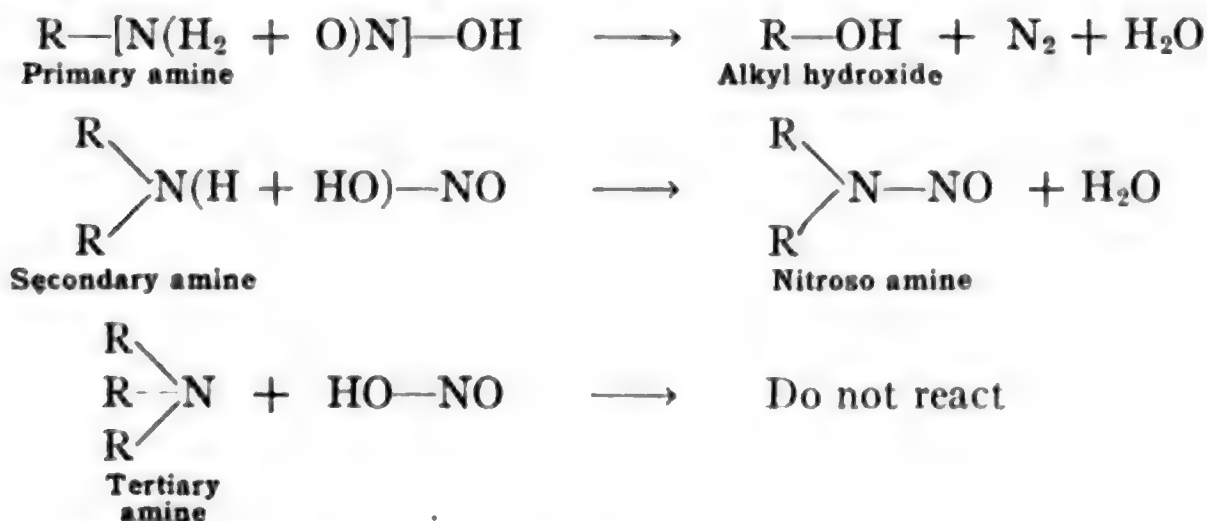
of the benzene series in Part II, that while the end products of the two reactions are of the same kind the **benzene** compounds do not form salts with nitrous acid, because they are less strongly basic. In this case, however, a most interesting class of intermediate products is formed which is not produced with the alkyl amines.

Secondary Amines, Nitroso Amines.—When a *secondary amine* reacts with nitrous acid the reaction is entirely different. A compound containing the group ($-\text{NO}$), in place of the one hydrogen of the amine and known as a *nitroso amine*, is formed.



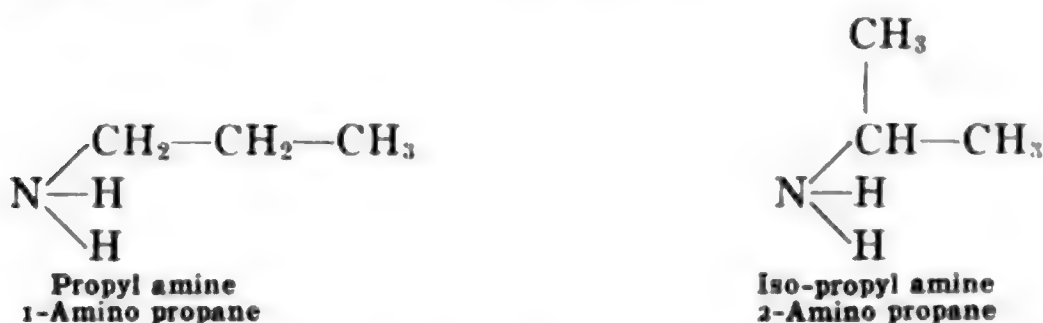
In the secondary amine there are *not two* remaining ammonia hydrogens and the reaction cannot take place as with primary amines. Instead, the *one* remaining ammonia hydrogen unites with the *hydroxyl* of the nitrous acid forming water, and the other product is the *nitroso amine*. These nitroso compounds are able to be distilled and can be reconverted into the amine by means of hydrochloric acid.

Tertiary Amines.—In the *tertiary amines* there is *no remaining ammonia hydrogen*, therefore, neither the primary nor secondary amine reactions can take place. The fact is that tertiary amines do not react with nitrous acid at all. We thus have a reaction which enables us to distinguish between primary, secondary and tertiary amines. Writing these reactions together we have

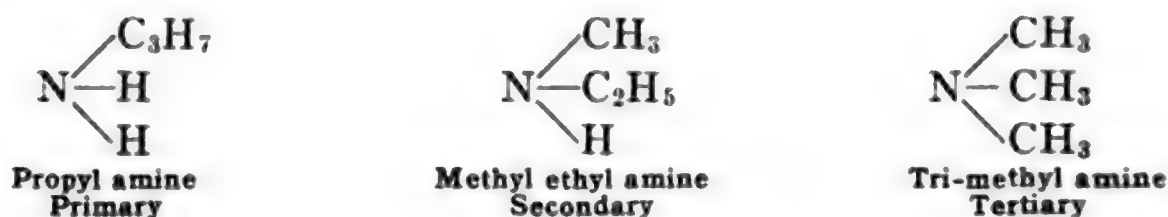


Isomerism.—The isomerism of the amines may be due to several things. *First*, it may be due to isomerism of the alkyl radical, and as

such will be of the same nature as the isomerism of the alkyl halides, *e.g.*, C_3H_9N may be



Such isomerism is possible in all three classes of amines. *Second*, it may be due to different alkyl groups whereby primary, secondary and tertiary amines become isomeric with each other, *e.g.*, the same empirical formula, C_3H_9N may be:



We thus have four isomeric amines of the formula C_3H_9N .

TABLE VIII.—HOMOLOGOUS SERIES OF ALKYL AMINES

Alkyl radical	Primary $R-NH_2$	Secondary $\begin{array}{c} R \\ \diagup \\ N \\ \diagdown \\ R \end{array} NH$	Tertiary $\begin{array}{c} R \\ \diagup \\ N \\ \diagdown \\ R \\ R \end{array}$
	B.P.	B.P.	B.P.
Methyl.....	- 6°	+ 7°	+ 3.5°
Ethyl.....	+ 19°	56°	90°
Propyl.....	49°	98°	156°
Iso-propyl.....	32°	84°	
Ethyl methyl.....	35°	
Hepta-decyl ($C_{17}H_{35}$).....	340° M.P. 49°		
Triacontyl ($C_{30}H_{61}$).....	M.P. 78°	

The highest members given are the highest known, and it will be noticed that they are solids. They are also insoluble in water, and are less basic and not like ammonia in their physical properties as are the lower members.

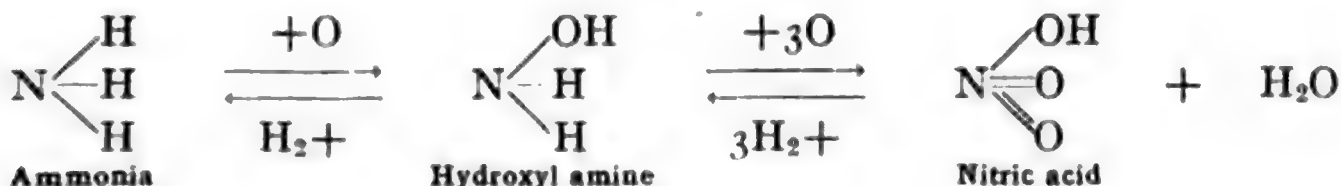
Methyl Amines

All three of the methyl amines are found naturally in herring brine, and in the dry distillation products of the residues obtained from fermented beet sugar molasses after it has been evaporated to drive off the alcohol and water. They also occur in certain plants and as the decomposition products of more complex nitrogenous organic substances such as morphine.

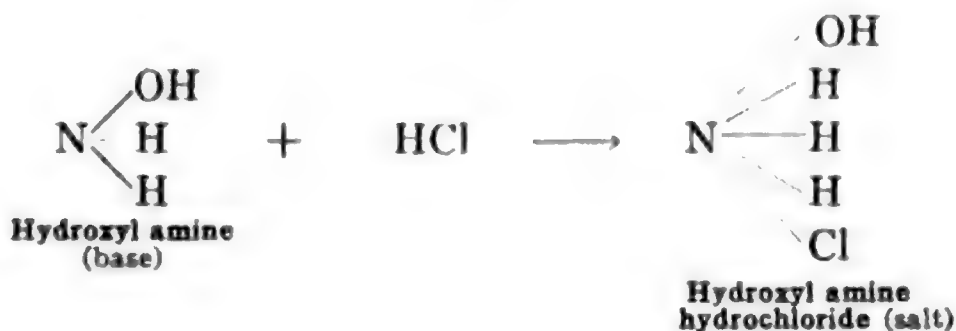
Hydroxylamine, Hydrazine, Hydrazoic Acid

Three compounds will now be given, two of which are closely related to the amines in that they are the simplest derivatives of ammonia which we know.

Hydroxyl Amine.—The first compound is an ammonia derivative, and is known as **hydroxyl amine**. When nitric acid is reduced by nascent hydrogen a compound is obtained, the composition of which is NH_2O and which proves to be a hydroxyl substitution product of ammonia, $\text{NH}_2\text{—OH}$ or **hydroxyl amine**. It may be looked upon as ammonia in which one hydrogen has been oxidized to hydroxyl. It thus stands between nitric acid and ammonia which are reciprocal oxidation and reduction products.



Hydroxyl amine is a hygroscopic liquid, readily soluble in water and possesses the basic and salt-forming properties of ammonia.



The salts are crystalline, soluble compounds. Hydroxyl amine is of especial importance in connection with the study of *aldehydes*, and will be mentioned again at that time.

Hydrazine.—The second compound is known as **hydrazine**, and is obtained by oxidizing **urea** or by reducing **hyponitrous acid**. It has the composition N_2H_4 , and is one of two compounds, other than ammonia, which contains simply nitrogen and hydrogen. It forms derivatives which prove it to be represented by the formula H_2N-NH_2 , which might also be called **di-amine** or **di-amide**. It was discovered in 1887 by **Curtius**. It may be looked upon as an amine substitution product of ammonia. It is similar to ammonia in its basic character and in its formation of a hydroxide base and salts. It is a crystalline compound, m.p. -1° and is soluble in water. Its derivatives, formed by replacing one or more hydrogens by alkyl or other hydrocarbon radicals, are the important compounds. **Phenyl hydrazine**, $C_6H_5-NH-NH_2$, is a derivative containing a hydrocarbon radical of the carbo-cyclic series of compounds known as *phenyl*, (C_6H_5-) . The importance of this compound, as of hydroxyl amine, will be seen when we study the *aldehydes*, and the *sugars*. **Di-methyl hydrazine**, $(CH_3)_2N-NH_2$ may also be mentioned.

Hydrazoic Acid.—The third compound, which is the other one containing only nitrogen and hydrogen, is not an ammonia derivative. It is known as **hydrazoic acid** or **tri-azoic acid**. Its formula is N_3H . It is a *mono-basic acid* while ammonia, NH_3 , is a base. It forms a salt with ammonia, NH_4N_3 , **ammonium hydrazoate**. Hydrazoic acid was also discovered by **Curtius** in 1890.

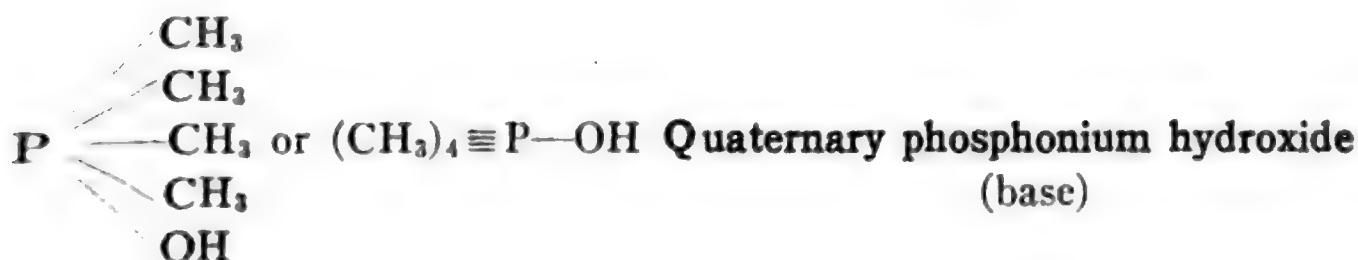
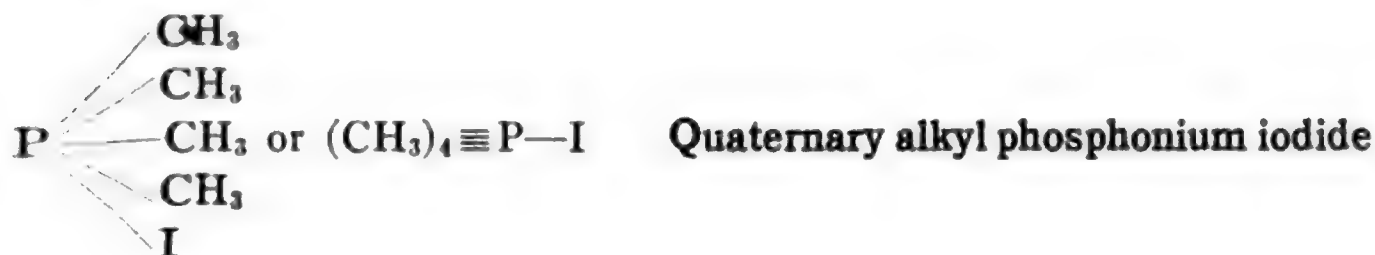
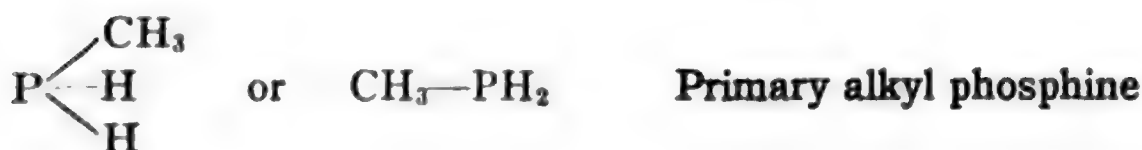
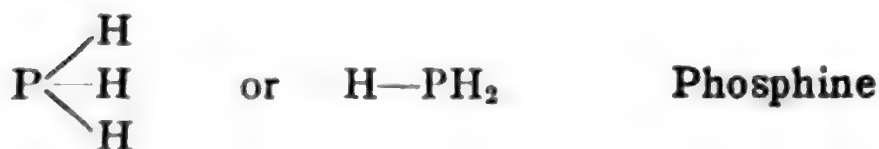
(C) PHOSPHORUS AND ARSENIC COMPOUNDS

I. PHOSPHINES $R-PH_2$

Phosphine, Phosphonium Salts.—It will be recalled from our study of inorganic chemistry that phosphorus forms a compound with hydrogen analogous to the nitrogen and hydrogen compound ammonia, NH_3 . It is given the formula in the gaseous state of PH_3 , and is called **phosphine**. This compound like ammonia forms salts with acids that are known as **phosphonium salts**.



Alkyl Phosphines and Phosphonium Compounds.—The simpler organic compounds of phosphorus are **alkyl phosphines** exactly analogous to the amines.

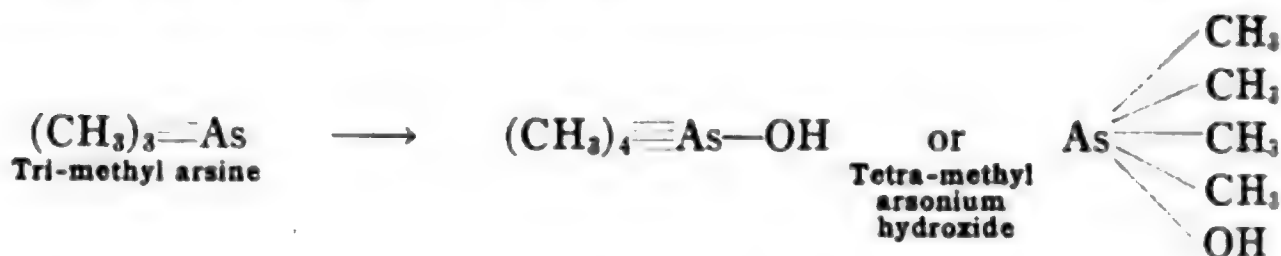


The primary, secondary and tertiary phosphines are weak bases, stronger, however, than the phosphine itself which is scarcely basic at all. The tetra-alkyl phosphonium hydroxides are strong bases.

II. ARSINES R—AsH_2

Corresponding arsenic compounds in which arsenic is united to alkyl radicals are derived from **arsine**, AsH_3 . The primary and secondary alkyl arsines are not known except as chlorine or oxygen

derivatives. The tertiary alkyl arsines, however, are strong bases forming salts analogous to the quaternary alkyl ammonium salts.



These arsenic compounds are known as *cacodyl* compounds. The radical $\left(\begin{smallmatrix} \text{CH}_3 \\ \text{CH}_3 \end{smallmatrix} \right) \text{As}-$ was called *cacodyl* by **Bunsen** who discovered it in 1839. It was given this name from *cacodus*, *stinking*, because compounds containing it possess an extremely bad odor. The oxygen derivatives of the methyl arsines are of especial interest because they were among the important compounds studied in the development of the radical theory. The *cyanogen radical* of **Gay Lussac**, the *benzoyl radical* of **Liebig and Wöhler**, and the *cacodyl radical* of **Bunsen** are always thought of in connection with the radical theory.

D. MONO-CYANOGEN SUBSTITUTION PRODUCTS

I. ALKYL CYANIDES R-CN ACID NITRILES

The next class of substitution products of the saturated hydrocarbons which we shall study are those formed from the alkyl halides by the action of potassium cyanide or silver cyanide.

Acids and Salts of Cyanogen.—We have been accustomed in inorganic chemistry to the group (CN) known as the *cyanide* or *cyanogen* group. The compounds which are generally treated as inorganic are **hydrogen cyanide** or **hydrocyanic acid**, HCN; metal salts of this acid, the metal cyanides, e.g., **potassium cyanide**, KCN, **silver cyanide**, Ag(CN), **mercuric cyanide**, Hg(CN)₂, **ferrous** and **ferric cyanides**. Fe''(CN)₂ and Fe'''(CN)₃; the double salts of potassium and iron, **potassium ferrocyanide**, K₄Fe''(CN)₆ or 4KCN.Fe''(CN)₂ and **potassium ferricyanide**, K₃Fe'''(CN)₆ or 3KCN.Fe'''(CN)₃ and finally the double salts of iron, corresponding to these potassium salts just given, e.g., **ferric ferrocyanide**, Fe'''₄(Fe''(CN)₆)₃ or 4Fe'''(CN)₃. 3Fe''(CN)₂ which is known as **Prussian Blue**, and **ferrous ferri-cyanide** Fe''₂(Fe'''(CN)₆)₂ or 3Fe''(CN)₂.2Fe'''(CN)₃ known as **Turnbull's Blue**.

These iron double salts are mostly blue in color, and it is from this fact that the group (CN) receives its name of *cyanogen* from the Greek word *cyanos* meaning *blue*. Hydrocyanic acid and the simple cyanide salts are analogous to the halogen binary acids and salts, and when oxidized they yield an oxygen acid and salts analogous to the oxygen containing chlorine compounds.

Acid	Salt	Oxidized Acid	Oxidized Salt
HCl	KCl	HOCl	KOCl
Hydrochloric acid	Potassium chloride	Hypochlorous acid	Potassium hypochlorite
H(CN)	K(CN)	HO(CN)	KO(CN)
Hydro cyanic acid	Potassium cyanide	Cyanic acid (unknown)	Potassium cyanate

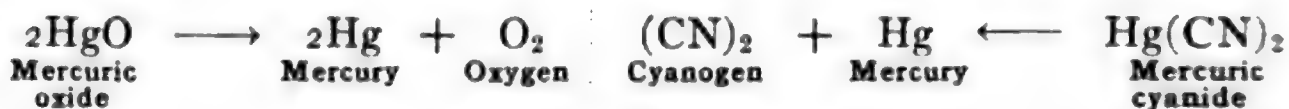
Relation to Organic Compounds.—It is a striking fact that whenever an organic animal or vegetable substance containing nitrogen is heated with metallic sodium the sodium compound of cyanogen is formed. There is no reason for supposing that all such organic nitrogen is present in the form of the cyanogen grouping but simply that on decomposition, under these conditions, nitrogen and carbon leave the compound, combined in this way. This reaction is used as a test for nitrogen in protein substances and may easily be made with such material as *hair*, *gelatin*, *egg albumin*, etc. It is also the basis of the commercial method for making potassium ferrocyanide, $K_4Fe(CN)_6$, which is prepared by heating substances containing nitrogen, *e.g.*, animal matter such as blood, etc., together with iron filings and potassium carbonate.



Potassium ferrocyanide by heating with K_2CO_3 is converted into potassium cyanide, KCN, and potassium cyanate, KOCN, and by oxidation with bromine or potassium bichromate yields potassium ferricyanide, $K_3Fe(CN)_6$. It is thus the starting point for all of the cyanogen compounds.

Whether the true place to study these compounds is in organic or inorganic chemistry will not be considered. As they have probably been taken up in connection with inorganic qualitative analysis they will simply be mentioned in order to introduce the alkyl cyanogen compounds which we shall now study. Later, however, all of the above mentioned cyanogen compounds together with sulphur analogues will be discussed in detail (p. 408).

Free Cyanogen.—When **mercuric oxide** is heated, **oxygen** is set free as a gas and metallic **mercury** is left. A similar change occurs when **mercuric cyanide** is heated. Mercury is left and a gas is given off which is extremely poisonous, colorless, soluble in water, and which burns with a blue flame. This substance is known as **cyanogen** and has the composition $(\text{CN})_2$.



Cyanogen Radical.—As stated at the beginning of this chapter, cyanogen substitution products of the hydrocarbons are formed when alkyl halides are treated with potassium cyanide. These compounds contain cyanogen as a substituting group or radical analogous to the halogen elements, and the radicals, *methyl* (CH_3) *amino* (NH_2), *hydroxyl* (OH), etc. A striking difference between the radical cyanogen and the methyl, amino and hydroxyl radicals is that the cyanogen radical is *known in the free condition*. The free substance, the gas **cyanogen**, probably bears the same relation to the radical cyanogen that a molecule of oxygen does to the atom.



When **methyl iodide** is treated with *potassium cyanide* a compound with the composition $\text{C}_2\text{H}_3\text{N}$ is formed by a simple reaction of metathesis. As this and many other reactions prove that both the methyl and the cyanogen radicals are present in the compound we express the reaction,



Carbon Linked to Carbon.—Do we know, however, that the cyanogen *carbon* is linked to the methyl *carbon* or is the *nitrogen* the linking atom? When methyl cyanide is boiled with water or alkalies **acetic acid** and **ammonia** are formed. In acetic acid, as we shall show later, there are two carbon atoms, the same as in methyl cyanide, and the two carbons are linked together. Therefore, *in methyl cyanide the cyanogen carbon is linked directly to the methyl carbon*.



Acid Nitriles.—This is a general reaction of alkyl cyanides or of any similar cyanogen substitution product so that whenever organic acids containing the same number of carbon atoms are formed from cyanogen compounds we know that the carbon of the cyanogen and not the nitrogen is the joining link. Because of this definite relation to acids the cyanides are known also and more generally as *acid nitriles*.

Relation to Amines.—When the alkyl cyanides are treated with nascent hydrogen an alkyl amine is formed in which the alkyl radical has *one carbon more* than the alkyl radical of the cyanide.



This is a general method for preparing amines, and affords another proof that carbon is linked to carbon in the alkyl cyanides.

II. ISO-CYANIDES $\text{R—N}\equiv\text{C}$ OR $\text{R—N}=\text{C}$

ISO-NITRILES OR CARBYLAMINES

Action of Alkyl Halides and Silver Cyanide.—The compounds formed by the reaction of alkyl halides with metal cyanides exhibit a new and peculiar case of somerism. When **silver cyanide**, instead of **potassium cyanide**, acts upon an alkyl halide there is formed a compound of the same composition as methyl cyanide, viz., $\text{C}_2\text{H}_3\text{N}$, but with distinctly different properties, *i.e.*, an isomeric compound. It is known therefore as **methyl iso-cyanide**. The explanation of the isomerism of these two compounds is furnished by the character of the products which they yield when decomposed with water. We have proven that in methyl cyanide the *methyl carbon atom is linked to the cyanogen carbon atom*.



In the products of this reaction the two carbons remain linked together in one compound while the nitrogen breaks away from the carbon and forms ammonia.

Nitrogen Linked to Carbon.—Now when the isomeric compound, formed with silver cyanide and the methyl halide, is decomposed with water the *nitrogen of the cyanogen remains linked to the methyl carbon* in the form of **methyl amine** and the other product contains the cyano-

gen carbon atom which has broken away from the nitrogen. The reaction is

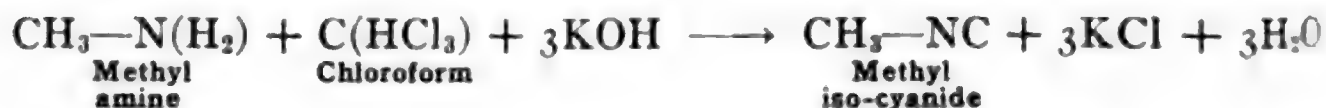


If there is no change in the linking of the other elements to the methyl carbon atom the formation of methyl amine, in which we know the methyl carbon is linked to nitrogen, proves that in the **methyl iso-cyanide** the *methyl carbon atom is linked to the nitrogen atom*. We should compare with this the formation of amines from the alkyl cyanides by the action of nascent hydrogen as given on the preceding page.



In this case the reaction proves that the methyl carbon is linked to the carbon atom of cyanogen and this carbon becomes a new chain carbon so that the alkyl radical of the resulting amine is *one carbon richer* than the alkyl radical of the cyanide.

Tests for Primary Amines.—The constitution of R—NC for the *isocyanides* is supported also by their synthesis from *primary amines*. When a primary amine, R—NH_2 , is treated with chloroform in alkaline solution an *iso-cyanide* is formed. **Chloroform** (p. 183), is **tri-chlor methane**, CHCl_3 . The reaction is,



The *two hydrogen atoms of the primary amine group*, together with the *one hydrogen atom of chloroform*, unite with the *three chlorine atoms of chloroform* to form hydrochloric acid leaving the *carbon atom of chloroform* to take the place of the *amine hydrogens* to form the *iso-cyanide*. In the *iso-cyanide* therefore the *methyl carbon atom must be linked to the nitrogen* as it is in methyl amine. The reaction becomes a specific test for *primary amines* inasmuch as two amine hydrogens are necessary to supplement the one of chloroform and form hydrochloric acid with the three chlorine atoms present. As *secondary amines* have only *one* remaining amine hydrogen atom and *tertiary amines* have *no* remaining amine hydrogen atom neither of these classes of amines are able to form isocyanides with chloroform. The fact is that *only*

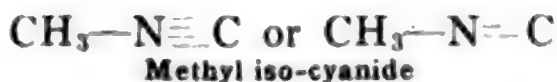
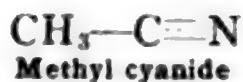
primary amines do so react and the reaction is a positive proof that the compound is of this class.

Hofmann's Iso-cyanide or Iso-nitrile Reaction.—As the iso-cyanides have a very characteristic odor, their formation is easily detected and the reaction is used as a test for primary amines.

It was discovered by **Hofmann** and is therefore known as the **Hofmann iso-cyanide or iso-nitrile reaction**. In this connection the other tests for primary, secondary and tertiary amines should be recalled (pp. 59–61).

Iso-nitriles, Carbylamines.—The alkyl cyanides because of their relations to acids are known as acid nitriles; methyl cyanide by hydrolysis yields **acetic acid** and it is thus known also as **acetic nitrile**. The iso-cyanides being isomeric with the nitriles are also termed **iso-nitriles**. Another name is sometimes used because of their amine relationship, viz., **carbyl-amine**; **methyl iso-cyanide**, $\text{CH}_3\text{—NC}$, being **methyl carbylamine**. The lower alkyl-iso-cyanides are liquids with a very strong disagreeable odor. They are readily hydrolyzed by water but form salts with hydrochloric acid and also with silver cyanide.

Nitrogen Carbon Linkage.—From their relationship to primary amines both by decomposition and by synthesis the constitution of the isocyanides is proven to be R—NC . Taking methyl cyanide and methyl iso-cyanide for illustration the formulas of these isomeric compounds are

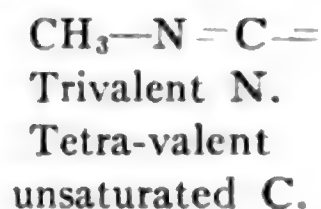
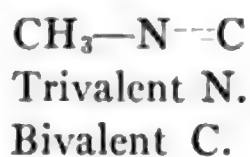
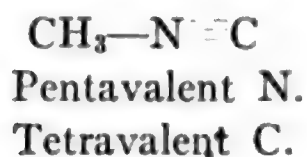


The exact nature of the linkage of the nitrogen between two carbons in the isocyanide has been explained in two ways.

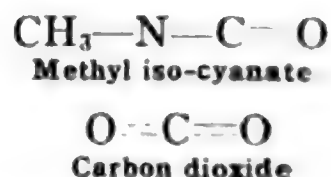
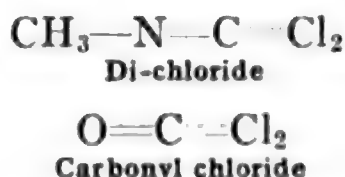
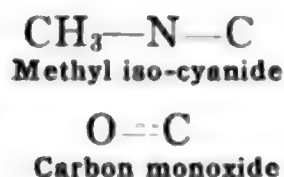
The first and until recently the accepted view is that in the cyanides nitrogen is *trivalent* while in the iso-cyanides it is *pentavalent* as shown in the above formulas. This is in accord with our assumption that in organic compounds carbon is *tetravalent*. It also agrees with facts in regard to the element nitrogen for we know that nitrogen frequently changes valence from *three* to *five*.

Bivalent Carbon.—Recent work on some derivatives of methane containing phenyl groups, related to the hydrocarbon **benzene** to be considered in Part II, have led to the view that carbon is not *always tetravalent* but that it may be *trivalent* or *bivalent*. If in the isocyanides nitrogen *remains trivalent* then *carbon* must become *bivalent* or else

the four valencies of the carbon are not all satisfied, *i.e.*, it is *unsaturated*. Methyl iso-cyanide may be either of the following:



Two reactions of the iso-cyanides have been used as supporting either of the last two formulas. Methyl isocyanide forms a compound, $\text{CH}_3\text{—N}=\text{C}=\text{Cl}_2$, which in turn by means of silver oxide yields **methyl iso-cyanate** the constitution of which is $\text{CH}_3\text{—N}=\text{C}=\text{O}$ as we shall presently show. These reactions are analogous to similar ones which occur with **carbon monoxide**, CO, a compound in which carbon is considered as bivalent.

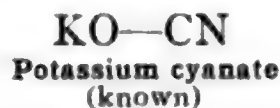
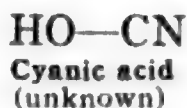
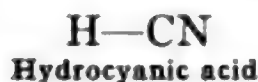
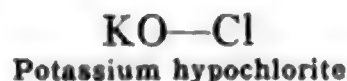
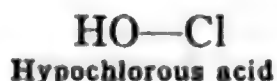
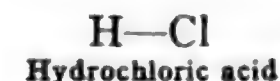


However, as other recent work has shown that oxygen may sometimes be *tetravalent* as well as *bivalent*, the above relationships between carbon monoxide, carbonyl chloride and carbon dioxide are possible of another explanation, *viz.*, that the *valence of oxygen changes while that of carbon remains constant as tetravalent*. In regard to the unsaturated condition of the carbon by which two valences are left unsatisfied we may simply say that such a condition is wholly different from unsaturation existing in compounds containing two carbons linked together and which we shall study later. It may also be questioned whether the condition existing when carbon has two unsatisfied valences is any different from that which exists in the case of bivalent carbon possible of changing to tetravalent. The whole problem of the exact nature of the linkage of the nitrogen in the iso-cyanides seems to be one connected with the change in valence of either nitrogen or carbon. If the nitrogen remains constantly *trivalent* the carbon must be the one that changes to *bivalent* while, if the carbon remains *tetravalent* the nitrogen must change from *trivalent* to *pentavalent*. The fact that the iso-cyanides show no resemblance to ammonium salts, whereas they are like the amines, indicates that it is probably carbon which changes and that in this compound it is *bivalent*.

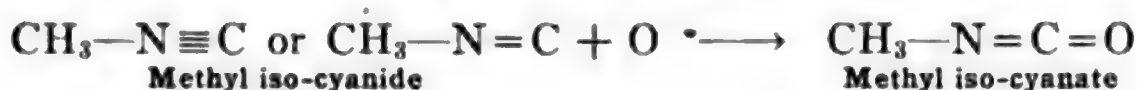
III. ALKYL ISO-CYANATES $R-N=C=O$

 THIO-CYANATES $R-S-C\equiv N$. ISO-THIO-CYANATES $R-N=C=S$

The isomerism existing in the case of cyanides or nitriles and isocyanides or iso-nitriles, which we have just discussed, is found also, in part, in their oxidation products the iso-cyanates and in analogous sulphur compounds the **thio-cyanates** and **iso-thio-cyanates**. We have referred to the fact that hydrocyanic acid like hydrochloric acid yields an oxygen acid which though unknown itself is represented by well known salts.

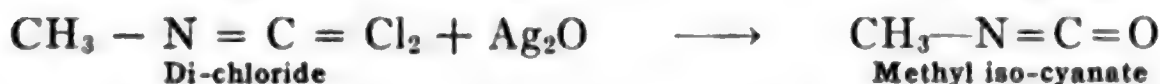


The alkyl derivatives of this cyanic acid, viz., *alkyl cyanates*, are not known for reactions which should yield them do not do so though there are obtained derivatives of the polymeric compound cyanuric acid (p. 418). The isomeric alkyl compounds or alkyl iso-cyanates are, however, known. These compounds may be made by the oxidation of the corresponding alkyl iso-cyanides.



The constitution of the alkyl iso-cyanates has been established as above by the following facts.

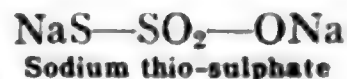
When hydrolized they yield *alkyl amines* in which the *alkyl radical is linked to nitrogen*; and they may be made, as previously stated (p. 72), from the iso-cyanides through the dichloride by means of silver oxide,



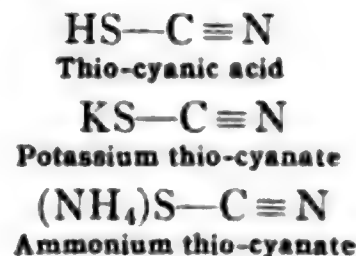
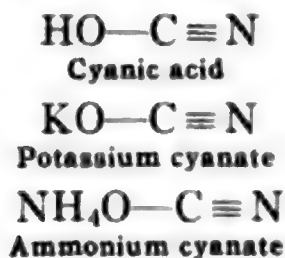
This relationship has already been discussed in connection with its bearing on the question of the existence of bivalent carbon in the iso-cyanides.

Thio-Compounds.—In inorganic chemistry we know compounds in which oxygen acids and salts have an **oxygen** atom replaced by **sul-**

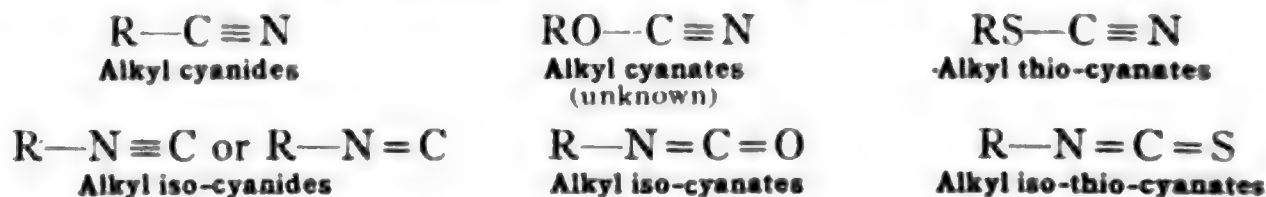
phur yielding *thio compounds*. The most common example of this is the case of **thio-sulphuric acid** and **thio-sulphates**.



This same substitution of sulphur for oxygen occurs in the case of cyanic acid and its salts, *e.g.*, **potassium thio-cyanate** and **ammonium thio-cyanate** used as reagents in testing for ferric iron.



Alkyl Thio-cyanates ; Alkyl Iso-thio-cyanates.—In the alkyl derivatives of thio-cyanic acid we again have isomerism exactly analogous to that in the unknown cyanates and the known iso-cyanates.



Alkyl derivatives of these cyanate compounds in which the alkyl radical is derived from a saturated hydrocarbon of the methane series are not of any special importance. When, however, we study another series of hydrocarbons known as the *unsaturated hydrocarbons* we shall find important derivatives which occur in nature. We shall then refer to this study of the general relationships which we have here discussed.

(E) NITRO COMPOUNDS R—NO_2

NITROSO COMPOUNDS R—NO

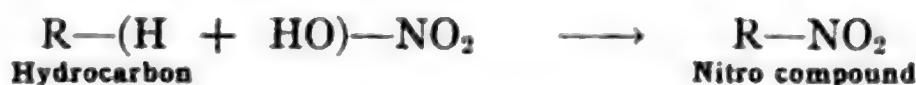
When ammonia is oxidized nitric acid is the result if the reaction is carried to its limit, but less complete oxidation produces nitrous acid.

Nitro Substitution Products.—Nitric acid is HO—NO_2 and nitrous acid is HO—NO . If these are reduced ammonia is the result. When the silver salt of nitrous acid acts upon an alkyl halide a reaction occurs similar to that of potassium cyanide upon the alkyl halides.

and a compound is formed in which the halogen of the halide is replaced by the group NO_2 .



This group (—NO_2), is the residue of nitric acid, HO—NO_2 , left when the acid hydroxyl is removed. It is known as the *nitro group*, and compounds containing it as *nitro compounds*. Some of the higher paraffin hydrocarbons yield nitro compounds when heated with dilute nitric acid under pressure by the reaction



In the paraffin series this reaction and the products formed are not of especial importance but we shall find that in the benzene or carbocyclic series the nitro compounds are easily formed directly from the hydrocarbons by action of nitric acid and they are very important compounds. When nitro methane is reduced by nascent hydrogen the *nitro group*, (—NO_2), the nitric acid residue, is *reduced* to the *ammonia residue*, (—NH_2). The result is an *alkyl amine*.



This is one of the general methods of forming primary amines.

Nitroso Compounds.—When nitrous acid itself, $\text{HO—}\ddot{\text{N}}\text{O}$, acts

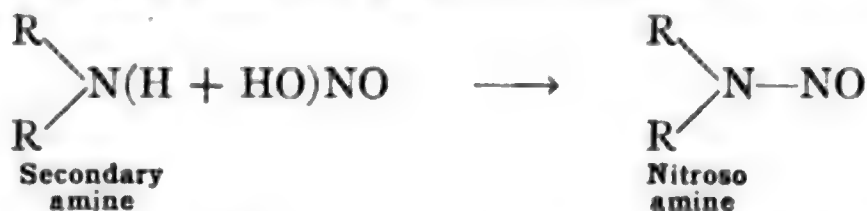
upon a tertiary hydrocarbon group, *i.e.*, the group $\begin{array}{c} \text{R} \\ \diagdown \\ \text{R} \text{—} \text{C} \text{—} \text{H} \\ \diagup \\ \text{R} \end{array}$ the hydro-

gen of the tertiary carbon group is removed together with hydroxyl of the nitrous acid, and a compound is formed containing the nitrous acid residue (—NO) known as the *nitroso group*. These compounds are analogous to nitro methane, but contain one oxygen less.



A similar reaction takes place also as we have recently discussed (p. 61) with the secondary amine group, the product in this case being

known as a *nitroso amine*. In both cases the reaction is with the one remaining hydrogen linked to carbon or nitrogen.



Nitroso compounds, like the nitro compounds, are converted into amines by reduction with hydrogen.

(F) METALLIC ALKYL COMPOUNDS—ORGANO-METALLIC COMPOUNDS

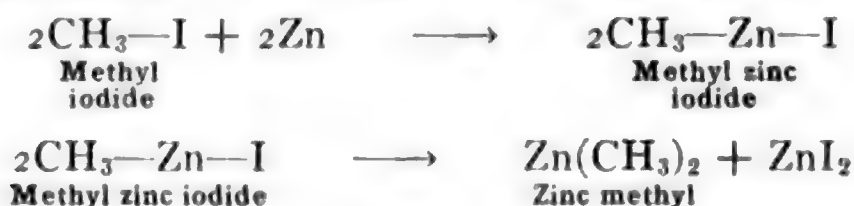
I. ZINC ALKYL $\text{Zn}-\text{R}$, ALKYL ZINC HALIDES $\text{R}-\text{Zn}-\text{I}$

Still one more class of alkyl derivatives should be mentioned in this part of our study. These are compounds of the alkyl radicals with metals, and are known in general as *organo-metallic compounds*. A large number of metals form compounds of this kind, and the ease of formation seems to have a definite relation to the position of the metal in the periodic system. Compounds of the alkali metals with organic radicals have not been isolated, but they probably exist as intermediate products and also as double compounds with other metallic alkyl compounds. The two groups of these compounds which we shall briefly consider are those of **zinc and magnesium**.

When zinc acts upon alkyl iodides in the **Frankland reaction** (p. 16), the final product, is a hydrocarbon composed of two of the alkyl radicals linked together.



Two intermediate products of this reaction can be isolated, and they have been shown to have the composition $\text{CH}_3-\text{Zn}-\text{I}$, **methyl zinc iodide** and $\text{Zn}(\text{CH}_3)_2$, **zinc methyl**. The reactions are:



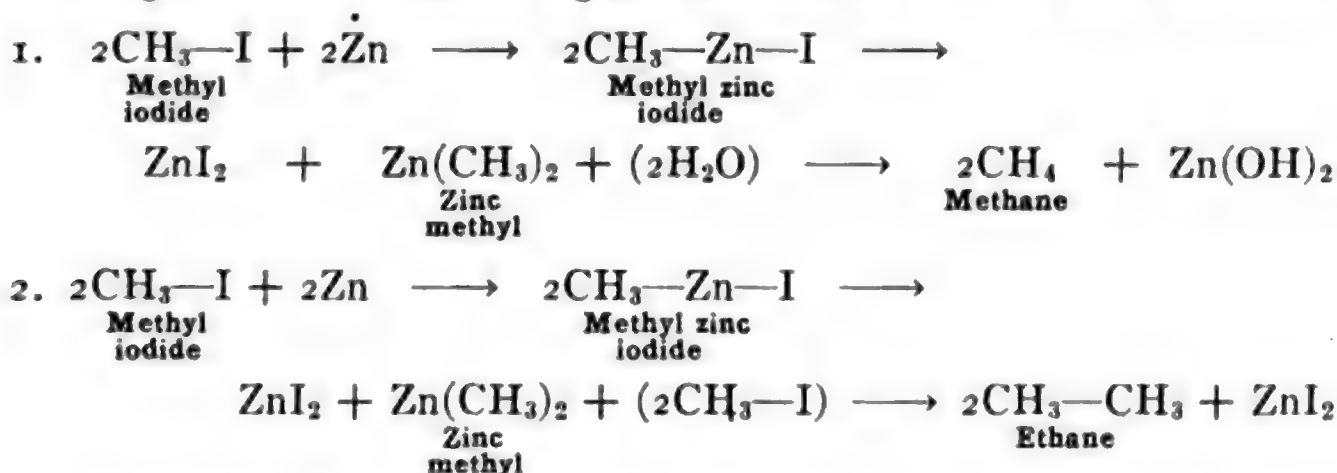
The zinc methyl then reacts with methyl iodide as follows:



Also the zinc methyl may react with water when a *lower hydrocarbon* is formed, viz., the one corresponding to the alkyl radical, in this case **methane**.



Writing out these reactions together in order to make it clear we have:



Frankland Reaction or Synthesis.—The discovery of the zinc alkyls was made by **Frankland** in 1850 and the reactions and syntheses above are known as the **Frankland Reaction**.

II. ALKYL MAGNESIUM HALIDES R—Mg—I

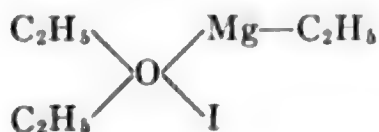
Grignard Reaction.—The magnesium alkyl compounds had been known but not used in synthetic reactions until 1899 when **Barbier** and in 1900 **Grignard** used them in this way. Since then the applications of the general reaction have been very numerous. It is known as the **Grignard Reaction** and may be illustrated as follows:



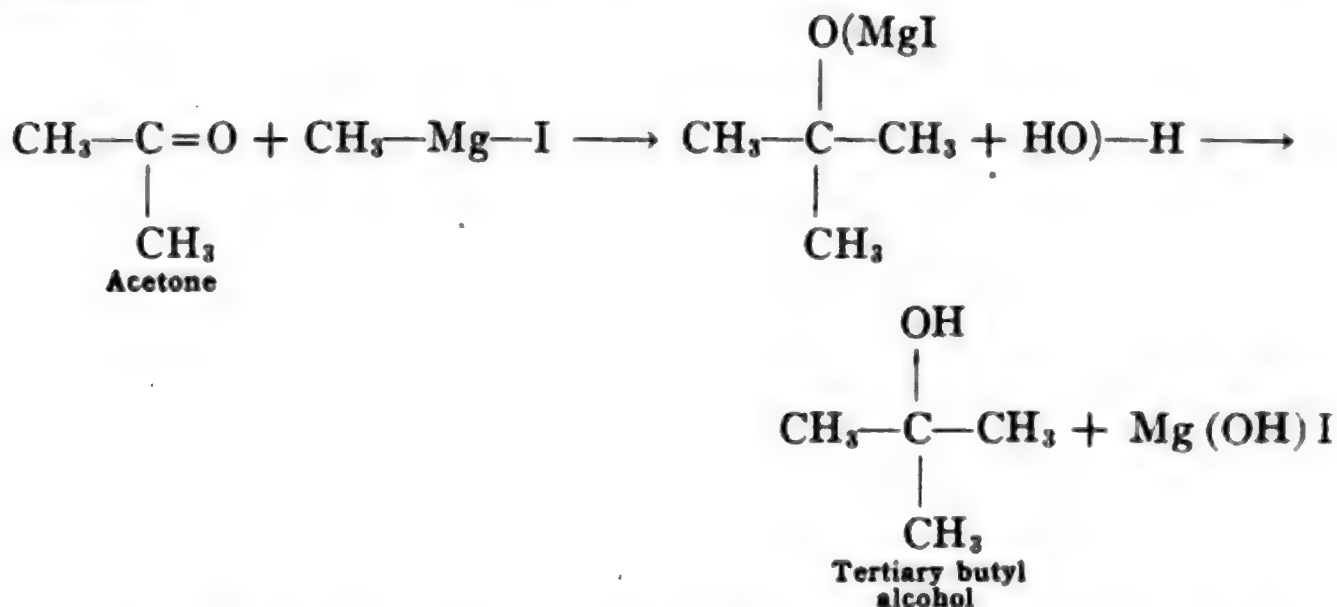
With water the ethyl magnesium iodide yields the hydrocarbon corresponding to the alkyl radical just as in the Frankland reaction, as follows:



¹ This compound is prepared in an ether solution, and it is believed that the ether enters into the product and that the formula is probably not the simple magnesium alkyl halide, but is



With compounds containing the carbonyl group ($=\text{CO}$), such as aldehydes, ketones or acid chlorides the alkyl magnesium halides react as follows:



These general reactions of the organo-metallic compounds in the **Frankland reaction** and the **Grignard reaction**, especially the latter, are applicable with modifications in a great variety of cases, so that by means of them alkyl radicals may be introduced into various desired positions. A further discussion of these reactions, at this time, is not necessary or desirable in this work, but they will be referred to in connection with certain compounds where they are especially important.

(G) MONO-HYDROXYL SUBSTITUTION PRODUCTS—ALCOHOLS

GENERAL

We come now to a series of compounds which has in it many well-known substances, and to which the class name of *alcohols* has been given. The two most common representatives of the series are ordinary alcohol or grain alcohol and **wood alcohol**. Both are valuable commercial substances, the former being obtained by the distillation of fermented grain or fruit, the latter by the distillation of wood, hence their names. The composition and empirical formulas of the two are similar, viz.,

Alcohol, $\text{C}_2\text{H}_5\text{O}$

Wood alcohol, CH_3O

Taking ordinary alcohol as typical of the entire series we may ask, how is it synthesized, how does it react with other substances, and what do these reactions show as to its constitution?

Alcohol not an Oxide.—In the first place the composition of alcohol, C_2H_6O , is striking, in that it consists of carbon and hydrogen in exactly the same ratio as in ethane, and in addition to this one atom of oxygen. This would seem to indicate that alcohol is a simple oxide of the hydrocarbon ethane, *i.e.*, $(C_2H_6)O$. Can we say, however, that ethane, or the ethane grouping itself is present in the molecule of alcohol, *i.e.*, are the six hydrogen atoms in alcohol in the same relation to the carbon as they are in ethane? Or, on the other hand, can we show positive proof that some other constitution is supported by facts? Several reactions do give this latter proof.

Reaction of Alcohol and Sodium.—When metallic sodium acts on alcohol, **hydrogen** gas is set free and a new compound known as **sodium alcoholate** is formed. The amount of hydrogen evolved is in the ratio of 1.008 parts by weight of hydrogen to 23.0 parts of sodium. That is, *one atom of hydrogen* is set free, and *one atom of sodium takes its place in the alcohol molecule*. The composition of the new compound is C_2H_5NaO . The important fact for our present consideration is that *only one hydrogen* is ever thus removed by sodium. Our proof that the six atoms of hydrogen in ethane are all alike in their relation to carbon is in the fact that one, two, three, four, five or six of them are possible of substitution by chlorine. Also when only one hydrogen is thus substituted by chlorine it makes no difference which one of the six is replaced for only *one* mono-chlor ethane, C_2H_5Cl , is known (p. 11). In alcohol it has never been possible to remove more than one hydrogen by means of sodium. Plainly, then, *one of the six hydrogen atoms in alcohol is different from the other five*. This might be indicated by writing the formula C_2H_5HO , and the reaction

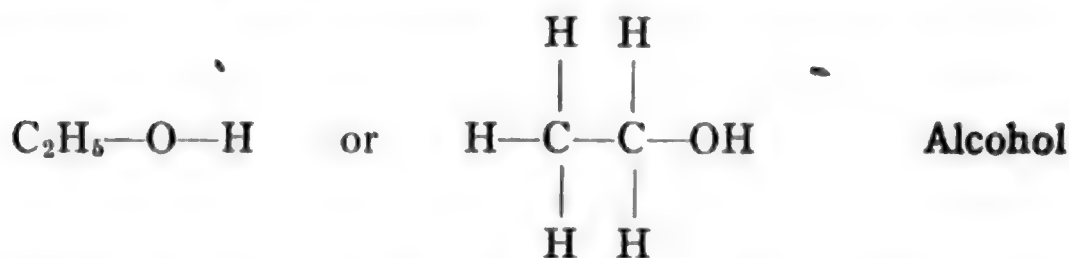


Now this reaction of alcohol and sodium is strikingly similar to the reaction of water and sodium. We write this latter reaction:

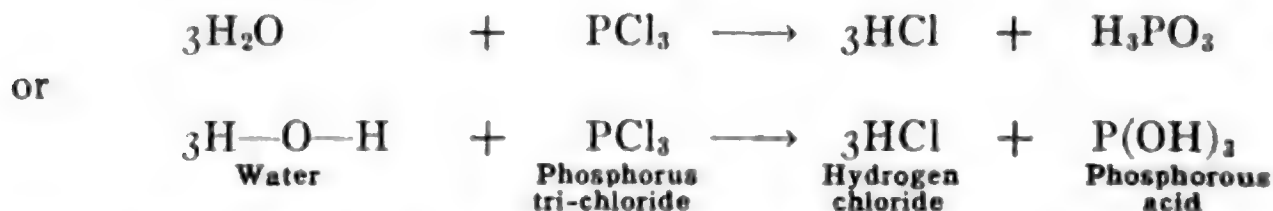


Water is considered as a combination of hydrogen and the group ($-OH$). There is, however, probably no difference in the hydrogen atoms, either one of them being removable, the other remaining in

combination with oxygen as OH. That is, water is H—O—H. If then the similarity of the reaction of alcohol and water indicates that the two compounds are similar in constitution the hydrogen atom of alcohol which is replaceable by sodium is *linked to the oxygen* rather than to the carbon. We may express this in our formula by



Reaction of Alcohol and Phosphorus Tri-chloride.—Three other reactions also prove that in alcohol we have the oxygen and hydrogen in the same grouping as in water, *i.e.*, as (—O—H). Two of these reactions are with the chlorides, or other halogen compounds of phosphorus. Using the chlorides for illustration there are two chlorides of phosphorus, viz., PCl_3 , **phosphorus tri-chloride** and PCl_5 , **phosphorus penta-chloride**. The first one, phosphorus tri-chloride, reacts with water as follows:



The chlorine of the phosphorus tri-chloride takes the place of the hydroxyl group of water, or, in other words, the phosphorus removes the hydroxyl and unites with it forming an hydroxyl compound, *i.e.*, P(OH)_3 or H_3PO_3 , **phosphorous acid**. When phosphorus tri-chloride reacts with alcohol the products of the reaction are found to be **ethyl chloride** and phosphorous acid, and we may write the reaction:



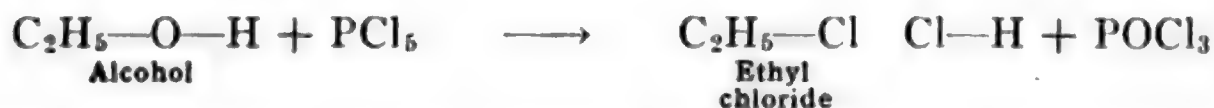
The two reactions then of phosphorus tri-chloride with water and with alcohol are exactly analogous. Phosphorous acid is formed in both cases due to the union of phosphorus with the (OH) group. In the case of water a compound of *hydrogen and chlorine* is the other product.

while with alcohol it is a compound of the radical *ethyl and chlorine*. If then we are correct in considering water as hydrogen linked to hydroxyl, *i.e.*, H—OH alcohol must be *ethyl linked to hydroxyl*, *i.e.*, $\text{C}_2\text{H}_5\text{—OH}$. The *hydrogen* in the water becomes the radical *ethyl* in alcohol, and the *hydroxyl* group is common to both.

When the other chloride of phosphorus, phosphorus penta-chloride PCl_5 reacts with water a reaction takes place, in which it is probable that *two chlorine atoms* from the penta-chloride exchange places with the *oxygen* of the water, two molecules of hydrochloric acid being thus formed.



Now with ethyl alcohol an exactly analogous reaction occurs and the products are phosphorus oxy-chloride, hydrochloric acid and the *chloride of the alkyl radical ethyl*. It must be, therefore, that the radical ethyl in alcohol occupies the place of one of the hydrogen atoms in water, the other hydrogen remaining as part of the hydroxyl group. The reaction is then,



These two reactions of the chlorides (or other halogen compounds) of phosphorus are characteristic of all compounds containing the hydroxyl group, and are used as proof of the presence of this group.

Reaction of Alcohol and Hydrobromic Acid.—The third reaction which proves the presence of the hydroxyl group in alcohol is with the halogen binary acids. When hydrochloric, or better hydrobromic or hydriodic acid, acts upon hot alcohol a partial decomposition of the alcohol takes place and the ethyl halide and water are formed



This reaction proves even more conclusively that water and alcohol are analogous compounds for in it the water is formed by exchanging the ethyl radical for hydrogen.

Synthesis of Alcohol from Alkyl Halides.—This is shown also in the converse way by the fact that in the reaction as given only a portion of the alcohol is converted into ethyl bromide because when a certain

amount of water has been formed the reaction *reverses* and the water reacts upon the ethyl bromide reforming alcohol and hydrobromic acid. The reaction is therefore written with the *double arrow which indicates its reversible character*. If, in the reverse reaction, some alkali, NaOH, is added with the water then the hydrobromic acid formed is neutralized to sodium bromide and the reaction therefore proceeds in one direction until all of the ethyl bromide is decomposed and converted into alcohol. This gives us a *general method of synthesizing alcohols from alkyl halides*.



The general discussion of such a reversible reaction and the methods of controlling it will be given later when we study the esters, (p. 140).

This synthesis of alcohols from alkyl halides takes place much better if instead of water we use another hydroxide, viz., **silver hydroxide**, AgOH, (moist silver oxide, $\text{Ag}_2\text{O} + \text{H}_2\text{O}$) which forms an insoluble silver salt with the halogen, the reaction thus proceeding in only one direction.



The group ($-\text{O}-\text{H}$) whether in **water**, $\text{H}-\text{OH}$, **sodium hydroxide**, $\text{Na}-\text{OH}$, **silver hydroxide**, $\text{Ag}-\text{OH}$, or **phosphorous acid**, $\text{P} \equiv (\text{OH})_3$, is a mono-valent group. This is because bivalent oxygen has only one valence satisfied by hydrogen, the other one remaining free, giving the group a valence of one. This group or radical which forms inorganic compounds known as *hydroxides* is known in organic chemistry as *hydroxyl*.

Alcohol of Crystallization.—One more reaction or property of alcohol which shows its similarity to water and which might, indeed, be much more conclusive if we understood more thoroughly the way water itself acts, is that alcohol like water forms crystalline compounds with certain anhydrous substances. In case of water we term it *water of crystallization*, so we may call its analogue *alcohol of crystallization*. Calcium chloride, CaCl_2 , forms crystals containing alcohol of crystallization.

Water Type Compounds.—Alcohol is thus a compound of the same general character as water, or as we may say, it belongs to the water

type. It is related to water in that the hydrogen is replaced by an organic radical. We may look upon the following four compounds as belonging to this type,

Water (hydrogen hydroxide)	H—OH	
Bases or alkalies (metal hydroxides)	Na—OH	or M—OH
Acids (oxygen acids) (non-metal hydroxides)	P—(OH) ₃	or NM—OH
Alcohols (alkyl hydroxides)	C ₂ H ₅ —OH	or R—OH

We shall find later that there are other groups of organic hydroxyl compounds known which are not alcohols. They are not, however, simple alkyl hydroxides.

Hydroxyl Substitution Products.—All of the preceding facts lead to the conclusion that alcohol is a compound in which the *ethyl radical* is linked to the *hydroxyl radical*, i.e., it is the *hydroxyl substitution product of ethane* or *hydroxy ethane*. Alcohols thus belong to the same general class of compounds as the halogen substitution products. The relationship between the hydrocarbons, the halogen substitution products, alkyl halides and the hydroxyl substitution products, alcohols, may be shown as follows:

Ethane	C ₂ H ₆ —H,	CH ₃ —CH ₂ —H,	$ \begin{array}{c} \text{H} \quad \text{H} \\ \quad \\ \text{H} - \text{C} - \text{C} - \text{H} \\ \quad \\ \text{H} \quad \text{H} \end{array} $
Ethyl chloride	C ₂ H ₅ —Cl,	CH ₃ —CH ₂ —Cl	$ \begin{array}{c} \text{H} \quad \text{H} \\ \quad \\ \text{H} - \text{C} - \text{C} - \text{Cl} \\ \quad \\ \text{H} \quad \text{H} \end{array} $
Ethyl alcohol	C ₂ H ₅ —OH,	CH ₃ —CH ₂ —OH,	$ \begin{array}{c} \text{H} \quad \text{H} \\ \quad \\ \text{H} - \text{C} - \text{C} - \text{OH} \\ \quad \\ \text{H} \quad \text{H} \end{array} $

The general formulas of these three groups of compounds being

$(\text{C}_n\text{H}_{2n+1})-\text{H}$ Hydrocarbons	$(\text{C}_n\text{H}_{2n+1})-\text{X}$ Alkyl halides	$(\text{C}_n\text{H}_{2n+1})-\text{OH}$ Alcohols
--	---	---

Methyl Alcohol.—The alcohol which we have used as an illustration of the group is the ordinary grain alcohol or **ethyl alcohol**, C_2H_5-OH . The other common alcohol is the one known as wood alcohol or **methyl alcohol** which, by reactions exactly similar to those we have been discussing, has been proven to bear the same relation to methane that ethyl alcohol does to ethane.

Methyl alcohol,	Wood alcohol,	<i>Hydroxy methane,</i>	CH_3-OH
Ethyl alcohol,	Alcohol,	<i>Hydroxy ethane,</i>	C_2H_5-OH

Homologous Series of Alcohols.—As hydroxyl substitution products of the hydrocarbons the alcohols form an homologous series analogous to that of the alkyl halides or halogen substitution products. Methyl and ethyl alcohol are thus the first two members of such a series derived from the methane or paraffin hydrocarbons.

Names of Alcohols.—According to the old system of nomenclature the alcohols were not named as hydroxyl substitution products, *e.g.*, ethyl hydroxide, thus making the names analogous to those of the alkyl halides. Instead of this the class name, *alcohol*, was used together with the name of the *alkyl radical* present. In some of the higher members of the series the numerical name for the radical was replaced by a name derived usually from the natural source of the alcohol. Thus **amyl**, **cetyl**, **ceryl** and **myricyl** alcohols for the *five*, *sixteen*, *eighteen* and *thirty* carbon compounds respectively. According to the official nomenclature the hydrocarbon name is simply changed by dropping the final *e* and adding the termination *ol*, indicating alcohol, thus, **methanol**, **ethanol**, **pentanol**, **hexanol**, etc.

The more important normal, primary alcohols of the series, with some of their physical constants are given in Table IX and in Table X are given the isomeric alcohols related to **propane** **butane** and **pentane** with the number of known and possible isomers of a few of the higher members.

Isomerism of the Alcohols.—As they are hydroxyl substitution products the isomerism of the alcohols is like that of the halogen substitution products, alkyl halides. This will be seen by examination of Table X. They possess the *normal* and *iso* together with the *primary*, *secondary* and *tertiary* characters (pp. 27, 49). We have spoken of isomerism of this kind as it occurs also in the isomeric hydrocarbons as *structural isomerism*. In the case of the hydrocarbons this isomerism is

TABLE IX.—NORMAL PRIMARY ALCOHOLS OF THE SATURATED SERIES

Common name	Official name	Formula	M.P.	B.P.	Sp. Gr.
				at 760 m.m.	at 0°
Methyl alcohol.....	Methanol.....	$\text{CH}_3\text{—OH}$	64.5°	0.812
Ethyl alcohol.....	Ethanol.....	$\text{C}_2\text{H}_5\text{—OH}$	−130°	78°	0.806
Propyl alcohol.....	Propanol.....	$\text{C}_3\text{H}_7\text{—OH}$	97°	0.817
Butyl alcohol.....	Butanol.....	$\text{C}_4\text{H}_9\text{—OH}$	117°	0.823
Pentyl or amyl alcohol.....	Pentanol.....	$\text{C}_5\text{H}_{11}\text{—OH}$	138°	0.829
Hexyl alcohol.....	Hexanol.....	$\text{C}_6\text{H}_{13}\text{—OH}$	157°	0.833
Heptyl alcohol.....	Heptanol.....	$\text{C}_7\text{H}_{15}\text{—OH}$	176°	0.836
Octyl alcohol.....	Octanol.....	$\text{C}_8\text{H}_{17}\text{—OH}$	195°	0.839
Nonyl alcohol.....	Nonanol.....	$\text{C}_9\text{H}_{19}\text{—OH}$	− 5°	213°	0.842
					at M.P.
Decyl alcohol.....	Decanol.....	$\text{C}_{10}\text{H}_{21}\text{—OH}$	+ 7°	231°	0.839
				at 15 m.m.	
Dodecyl alcohol.....	Dodecanol....	$\text{C}_{12}\text{H}_{25}\text{—OH}$	24°	143°	0.831
Tetradecyl alcohol..	Tetradecanol..	$\text{C}_{14}\text{H}_{29}\text{—OH}$	38°	167°	0.824
Hexadecyl or cetyl alcohol.....	Hexadecanol	$\text{C}_{16}\text{H}_{33}\text{—OH}$	50°	190°	0.818
Octadecyl alcohol...	Octadecanol..	$\text{C}_{18}\text{H}_{37}\text{—OH}$	59°	211°	0.813
Ceryl alcohol.....	Heptacosanol	$\text{C}_{27}\text{H}_{55}\text{—OH}$	76°		
Myricyl alcohol.....	Triacontanol..	$\text{C}_{30}\text{H}_{61}\text{—OH}$	86°	0.808

due entirely to a *difference in the chain of carbons* present in the compound. In the case of the halogen and hydroxyl substitution products the hydrocarbon chain may remain the same, and isomerism may be due to the *different position in which the halogen or hydroxyl enters the chain*. To illustrate with four of the isomeric pentanols.

Pentanol-1, $\text{CH}_3\text{—CH}_2\text{—CH}_2\text{—CH}_2\text{—CH}_2\text{OH}$

Pentanol-2, $\text{CH}_3\text{—CH}_2\text{—CH}_2\text{—CH(OH)—CH}_3$

2-Methyl butanol-4, $\text{CH}_3\text{—CH—CH}_2\text{—CH}_2\text{OH}$



2-Methyl butanol-3, $\text{CH}_3\text{—CH—CH(OH)—CH}_3$



TABLE X.—ISOMERIC ALCOHOLS (PROPYL, BUTYL, PENTYL, ETC.)

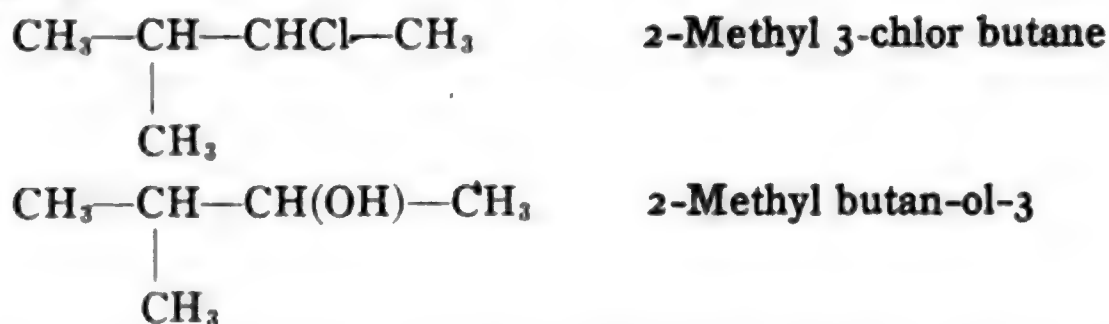
Common or older name	Official name	Formula	B.P.	Sp. Gr. at 20°
Propyl alcohols	Propanols			
Primary.....	Propanol-1.....	$\text{CH}_3\text{—CH}_2\text{—CH}_2\text{—OH}$	97°	0.804
Secondary.....	Propanol-2.....	$\text{CH}_3\text{—CH(OH)—CH}_3$	81°	0.789
Butyl alcohols	Butanols			
(Normal) primary.....	Butanol-1.....	$\text{CH}_3\text{—CH}_2\text{—CH}_2\text{—CH}_2\text{—OH}$	117°	0.810
(Normal) secondary.....	Butanol-2.....	$\text{CH}_3\text{—CH}_2\text{—CH(OH)—CH}_3$	100°	
(iso-primary).....	2-Methyl propanol-1.....	$\text{CH}_3\text{—CH—CH}_2\text{—OH}$ CH_3	107°	0.806
Iso-(tertiary).....	2-Methyl propanol-2.....	$\text{CH}_3\text{—C(OH)—CH}_3$ CH_3	83°	0.786
Pentyl or amyl alcohols	Pentanols			
(Normal) primary.....	Pentanol-1.....	$\text{CH}_3\text{—CH}_2\text{—CH}_2\text{—CH}_2\text{—CH}_2\text{—OH}$	138°	0.815
Iso-amyl.....	2-Methyl butanol-4.....	$\text{CH}_3\text{—CH—CH}_2\text{—CH}_2\text{—OH}$ CH_3	131°	0.810
(iso-primary).....	2-Methyl butanol-1.....	$\text{CH}_3\text{—CH}_2\text{—CH—CH}_2\text{—OH}$ CH_3	128°	
Active amyl.....	Pentanol-2.....	$\text{CH}_3\text{—CH}_2\text{—CH—CH(OH)—CH}_3$ CH_3	119°	
Methyl propyl carbinol.....	2-Methyl butanol-3.....	$\text{CH}_3\text{—CH—CH(OH)—CH}_3$ CH_3	112°	
(Normal secondary).....	Pentanol-3.....	$\text{CH}_3\text{—CH}_2\text{—CH(OH)—CH}_2\text{—CH}_3$	117°	
Methyl iso-propyl carbinol.....	2-Methyl butanol-2.....	$\text{CH}_3\text{—C(OH)—CH}_2\text{—CH}_3$ CH_3	102°	
(iso-secondary).....	2-2-Di-methyl propanol-1.....	$\text{CH}_3\text{—C—CH}_2\text{—OH}$ CH_3	112°	

Seventeen hexanols are possible (8 primary, 6 secondary, 3 tertiary). Of these 14 are known. Of the heptanols there are 38 possible isomers and 14 are known. Nine octanols, 6 nonanols and 5 decanols are known.

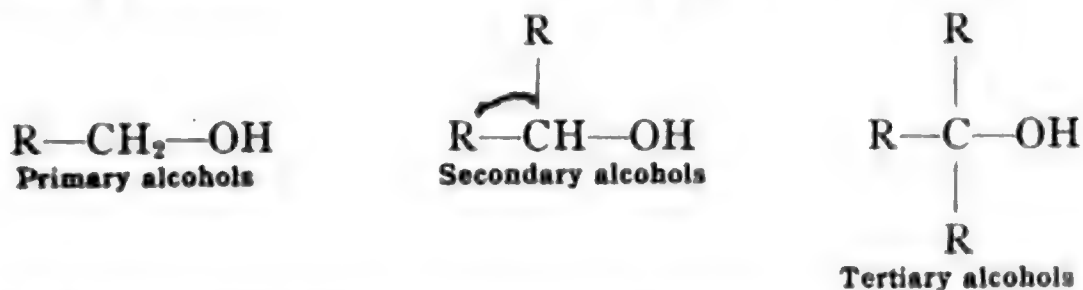
The above formulas represent different isomers because the chain hydrocarbon is normal or straight in two cases, and iso or branched in the others, as shown in the vertical pairs of formulas. On the other hand difference in structure results because the hydroxyl is substituted in a different carbon group, as shown in the horizontal pairs of formulas.

Now the first kind of structural isomerism is called *root isomerism* or *chain isomerism* and is the only kind present in the case of hydrocarbons. The second is known as *position isomerism* and is possible in all substitution products of the hydrocarbons. Both are, however, included in the term *structural isomerism*.

Names of Isomeric Alcohols.—The naming of isomeric alcohols follows the same plan as that of the isomeric alkyl halides. In the latter, however, the halogen as well as the substituting alkyl radical is considered as a substituting group in the chain of carbons which gives the name to the compound, viz., the longest straight chain of carbon atoms present. In the alcohols the hydroxyl group is considered a part of the chain name, which, therefore, takes the alcohol termination. The position of the hydroxyl is designated by a number as in other cases. This will be clear from the following examples in which hydroxyl and chlorine are substituted in the same hydrocarbon and in the same position.



The names of the isomeric alcohols in Table X will thus be clearly understood. The position isomerism gives rise to the primary, secondary and tertiary alcohols characterized by the groups,



This is exactly analogous to primary, secondary and tertiary alkyl halides as discussed under those compounds (p. 47).

Stereo Isomerism

Optical Activity.—We come now, in the case of the isomeric alcohols, to a new and most interesting example of isomerism. The five carbon alcohol 2-methyl butanol-1, differs from the other seven structurally isomeric amyl alcohols not only in structure, but also in other striking ways. *Three* different amyl alcohols are known all of which have the constitution of **2-methyl butanol-1**. Two of these three are known as *optically active*, all the other amyl alcohols being *inactive*. Certain substances either in the crystalline form, as in the case of quartz; in solution, as in the case of **sugar**; or in the liquid form, as in the case of the alcohol we are considering; possess this physical property of optical activity. This property is shown by the fact that the compound has the power to *turn or rotate* the plane of vibration of a ray of light that has been polarized.

Dextro, Levo and Inactive Compounds.—All optically active substances rotate the plane of polarized light either in one direction to the *right* or in the contrary direction to the *left*. On this account they are known as *right-handed or dextro-rotatory and left-handed or levo-rotatory*. The phenomenon of polarization being purely a physical one will not be discussed here. An explanation of it may be found in text books of physics or in chemical books which consider in detail such subjects as the sugars. All that need be added is that optically active compounds are readily examined by means of an instrument known as a *polariscope* and the direction of rotation (*right or left*) and the exact amount of rotation in degrees may be accurately determined.

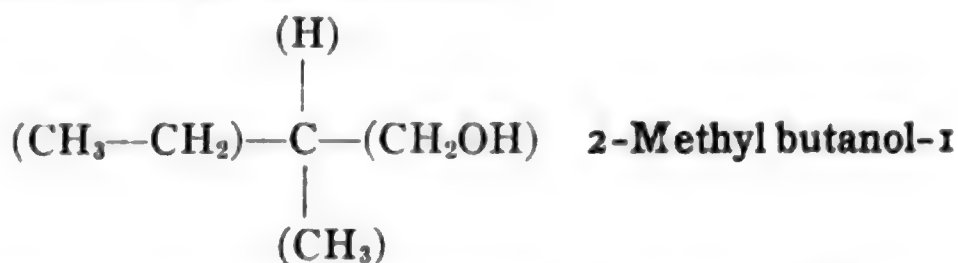
What we are concerned with at this time is an explanation on chemical grounds of the important fact that *three amyl alcohols, or pentanols, are known all of which possess the same structural formula, viz., 2-methyl butanol-1*; and that one of these compounds is *dextro-rotatory*, another is *levo-rotatory* and the third one is *inactive*. These three are different individual compounds with practically the same physical properties other than optical. The inactive variety of **2-methyl butanol-1** differs, however, from the other seven structurally isomeric pentanols which are likewise inactive not only in its structure but also in the fact that by means of certain reactions there may be obtained from it both the dextro-rotatory and the levo-rotatory compounds. In it, and in other inactive compounds of the same kind, *there are present equivalent amounts of the two oppositely active compounds*.

the *inactivity* being due to a balancing of one activity by the other. When the two active compounds are obtained, as above, from the inactive one we say that the inactive compound has been *split into its two optical components*. The other seven inactive amyl alcohols have never been thus split into optical components.

Pasteur.—The discovery that optically active substances exist in two forms *dextro-rotatory*, and *levo-rotatory* and that the corresponding *inactive compound* is composed of equal amounts of the dextro and levo and may be split into these two forms, was made by **Pasteur**, who, because of his later remarkable work in the field of pathology, is not generally known as a chemist. **Pasteur** made this discovery during a study of **tartaric acid**, and it will be spoken of again when we come to that compound.

Though we can thus explain the existence of these three alcohols which possess the structural formula of **2-methyl butanol-1** we do it in each case only in terms of the other two, *i.e.*, the inactive compound consists of a mixture of the dextro and levo forms and conversely. How then can we account for the fact that the two active isomers and, therefore, the three together are possible with the same structural formula?

Theory of van't Hoff-LeBel.—Two men independently of each other advanced a theory which explains these facts. One, a Dutch chemist by the name of **van't Hoff**, and the other a French chemist, **LeBel**. On examining the structural formulas of optically active compounds these men each saw that they differed in a common way from all optically inactive compounds which were not possible of being split into optical components. Taking as an illustration the alcohol with which we are dealing, *viz.*, **active amyl alcohol** or **2-methyl butanol-1** we see by examining its formula that one of the carbon atoms is characteristically different from all of the others.



Carbon atom 2 has linked to it a *methyl* group ($-\text{CH}_3$), a hydrogen atom ($-\text{H}$), a *primary alcohol* group ($-\text{CH}_2\text{OH}$), and an *ethyl* group (CH_3-CH_2-), *i.e.*, there are *four different groups or atoms* linked to

this one carbon. It is the only carbon in the molecule having such relations.

Asymmetric Carbon.—Now **van't Hoff** and **LeBel** found that *all optically active compounds contained at least one such carbon atom.* They ascribed the existence of two optically active forms to the presence in the compound of this unsymmetrically related or asymmetric carbon atom. The asymmetry of the compounds, in that one form is dextro-rotatory the other levo-rotatory, is due to this asymmetric arrangement of the molecule in space. We emphasized the fact that our structural formulas as we have been using them are simply plane representations of relationships, and indicate nothing as to the arrangement in space of the atoms or groups in a molecule. The theory of **van't Hoff** and **LeBel** considers the molecule as it is arranged in space. The isomerism so explained is known as *stereo-isomerism* or *space isomerism*.

Stereo-isomerism.—According to **LeBel** the simple fact that a molecule is built up asymmetrically in space will explain all cases of optically active compounds existing in the three forms mentioned. An arrangement unsymmetrical on one side would explain a dextro form and the arrangement unsymmetrical on the other would explain the levo form, a mixture of an equal number of molecules of the two forms being inactive. He assumed no definite arrangement for the space relations of the atoms or groups. **van't Hoff**, however, with the same idea, went a step further and devised a definite geometrical arrangement of the atoms in space which would explain the asymmetry and thus the three isomeric compounds.

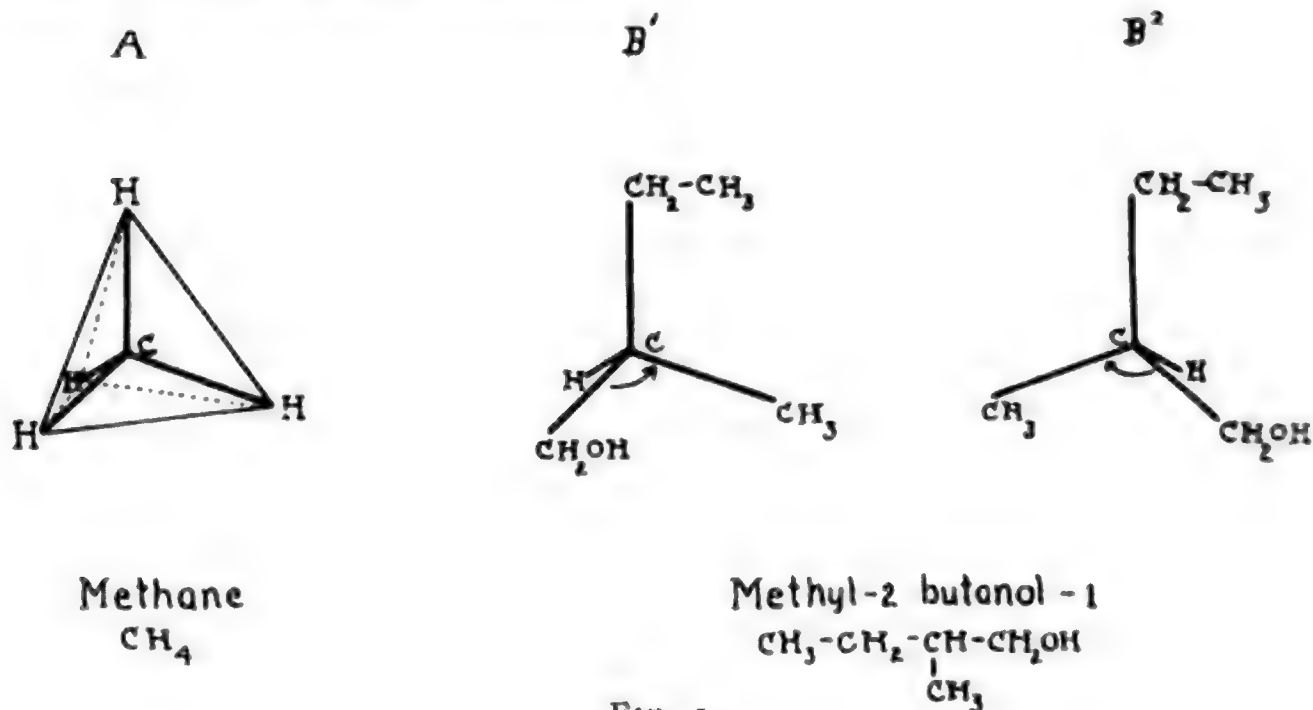


FIG. 1.

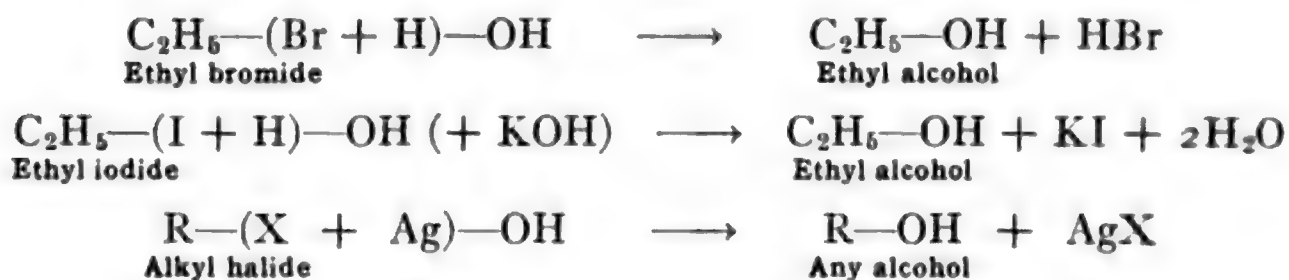
Tetra-hedral Carbon.—He assumed that carbon with its four equal valencies *exists in space as though situated at the center of a regular tetra-hedron* with four lines of valence each directed toward an apex. If in such an arrangement the atoms or groups linked to a carbon atom to form a molecule are all alike as in the case of methane, no other possible form can be given to the molecule than that given above in *A*. If, however, as is true in the case of active amyl alcohol and of all similar optically active compounds, the four groups linked to a carbon atom are all different the suggested tetrahedral formula shows immediately how *two* and *only two* arrangements are possible as represented in the figures *B*¹ and *B*². It will be observed that the two forms resulting are related to each other as the *right hand* is to the *left*, or as an *object* is to its *image*. They are not possible of being superimposed upon each other and are what **Pasteur** termed *enantiomorphic forms* or *enantiomorphs*.

Enantiomorphs.—A molecule possessing the arrangement in space represented by *B*¹ would, because of its asymmetry, be conceivable of being unsymmetrical in relation to polarized light, and could rotate the plane, let us say, to the *right*. A molecule arranged as in *B*², however, would necessarily have an opposite effect upon polarized light, *i.e.*, it would rotate the plane to the *left*. A compound composed of molecules *B*¹ would thus be *dextro-rotatory*, and one composed of molecules *B*² would be *levo-rotatory*. If, however, a compound was composed of an *equal number of molecules B*¹ and *B*² it would be *inactive* to polarized light because the effect of each molecule would be balanced by the effect of its counterpart molecule. We would have, therefore, three compounds possessing exactly the same structure but differing optically because of the asymmetric nature of one of the carbon atoms present. All compounds, furthermore, which contained one or more asymmetric carbons would as a result be active toward polarized light, and would exist in at least these three forms.

This then, is the **van't Hoff-LeBel Theory of Stereo-isomerism** known also as the *Theory of the Asymmetric Carbon Atom* or as the *Tetrahedral Theory*. The theory is supported by a large number of facts and has been fruitful in leading to new discoveries. We shall find cases of stereo-isomerism in several of the classes of compounds which we shall study and some of our most common substances, such as **lactic acid**,

tartaric acid and the **sugars**, can be understood only in the light of this theory. It is one of the several fundamental conceptions on which the whole structure of organic chemistry rests. The methods by which the inactive form of stereo-isomeric compounds may be separated into its optical components will also be considered at length when we study **tartaric acid** as it was in connection with his epoch-making investigation on this substance that **Pasteur** first made such a separation.

Alcohols, General Methods of Preparation.—The general methods for the preparation of the alcohols, so far as they involve compounds which we have already studied, resolve into one method which has been discussed already in connection with the proof that alcohols are hydroxyl substitution products of the hydrocarbons. This is the synthesis from alkyl halides by means of water in the presence of alkalis or in excess with heat and by means of moist silver oxide, (AgOH).



This method, of course, always yields the alcohol corresponding to the hydrocarbon which is the mother substance of the alkyl radical of the halide used. The alcohol will contain the same number of carbon atoms as the alkyl halide, and it will possess the same structure. The reaction is accomplished in the first case with water by heating the halide with much water at $100^\circ\text{--}200^\circ$, the excess water preventing the reversion of the reaction, or by heating with water in the presence of alkalis to neutralize the acid formed. With silver hydroxide the reaction takes place at ordinary temperatures and is non-reversible. Lead hydroxide may also be used. As was stated under the alkyl halides the alkyl iodide is the halide most used because it is the most active.

General Properties.—From Tables IX and X the homologous nature of the series of alcohols can readily be seen to be of exactly the same character as in the case of the hydrocarbons and alkyl halides. The rising of the boiling point in the normal series and the falling in each

isomeric group holds here as with alkyl halides. The boiling points of the alcohols compared with the hydrocarbons is higher, the lowest member, **methanol** or **methyl alcohol**, being a liquid at ordinary temperatures, boiling at 64.5° . The first three members, **methyl**, **ethyl** and **propyl alcohols** are limpid liquids with a pleasant odor and burning taste, being more or less poisonous, especially when concentrated. They burn readily, the lower members with a colorless flame. They are easily soluble in water, mixing with it in all proportions and from which they may be separated by distillation or by the addition of a readily soluble salt, *e.g.*, potassium carbonate or calcium chloride or a dehydrating substance like quick lime, CaO . As we go up the series the boiling point rises and the solubility in water decreases. From **butanol** to **decanol** they are oily liquids with unpleasant odor, and only the first is soluble in water in an appreciable amount (12 parts). Above the tenth member they are solid, wax-like substances without odor, insoluble in water, but soluble in ethyl alcohol or ether from which they may be crystallized.

Natural Occurrence.—Alcohols occur very widely distributed in the plant kingdom, but not in the free condition. It has been claimed that ethyl alcohol has been found free in plants but this is doubtful. In combination with other substances, however, they are found in many plants and also in animals. The compounds in which they occur are known as *esters* or *ethereal salts* and are prepared by the reaction of alcohols with organic acids. These compounds will be discussed fully a little later. At present it is sufficient to say that **fats**, **oils** and **waxes** and some of the aromatic or essential oil constituents of plants are compounds of this kind. When these substances are boiled with dilute alkalies the alcohol is set free and may be obtained as such. We may mention two examples: *oil of wintergreen* yields **methyl alcohol**, **methanol**; *spermaceti* yields **cetyl alcohol**, **hexadecanol**. Besides being present in this form in plants and animals, several of the most important alcohols are obtained either by direct distillation of vegetable material, as in the manufacture of methyl alcohol by the dry distillation of wood, or by the distillation of the product of the fermentation of vegetable materials, as in the manufacture of ethyl and amyl alcohols by the fermentation of the sugar found free, or formed from the starch, in fruit or grain.

Methyl Alcohol Methanol Wood Alcohol

Manufacture from Wood.—As its common name signifies this simplest of the alcohols is prepared by the dry distillation of wood. When wood is heated out of contact with oxygen (air) carbon is left in the form of charcoal as one of the products of the decomposition of the organic compounds present in the wood. The other products of the decomposition are volatile substances consisting of gases and liquids. The former consist largely of hydrocarbons. The liquid portion consists of a low boiling light liquid of acid character and known as *wood spirits* or *pyro-ligneous acid*, and a high boiling thick liquid known as *wood tar*. The pyroligneous acid, which is also termed *crude wood vinegar*, contains several compounds in the form of water solution. The three most important ones are **methyl alcohol**, **acetic acid** and **acetone**. After neutralizing the acid by means of an alkali, usually lime or chalk, the liquid is redistilled. The acetic acid is held back as the non-volatile calcium salt while the methyl alcohol with some of the other constituents distils over. Water is then added to the distillate in order to separate out some oily hydrocarbons and the solution is again distilled. In this last distillation a tall still, known as a column still, is used by means of which the liquid undergoes fractionation and a distillate is obtained containing a high per cent of methyl alcohol. The best product so obtained is known as *Columbian Spirits* and contains about 95 per cent methyl alcohol, the remainder being water and traces of other compounds. To secure absolute or 100 per cent methyl alcohol the 95 per cent product is treated with calcium chloride. With the alcohol, this salt forms a crystalline compound which is separated and purified and then treated with sulphuric acid and converted back into the alcohol. A similar method is to convert the alcohol into a compound formed with oxalic acid. This is purified and then decomposed with water. Crude pyroligneous acid usually contains about 2 per cent of methyl alcohol. The wood used in the manufacture of methyl alcohol and the other products mentioned is one of the hard woods, e.g., maple, birch, beech, oak and hickory. The yield of alcohol is higher the lower the temperature of distillation. It averages about 0.5 to 0.8 per cent. The annual consumption of wood in this industry in the U. S. in 1916 was estimated at about 1,100,000 cords. From one

cord there is obtained about 9.9 gallons of 82 per cent methyl alcohol so that the total production was about 10 to 11 million gallons.

From Beet Sugar Residues.—Another source for the manufacture of methyl alcohol is the residue from beet sugar manufacture known as *vinasse*. When beet sugar is refined the molasses from which all possible sugar has been crystallized is allowed to ferment and the liquid then distilled. The residue left from this distillation is then dry distilled and methyl alcohol is obtained just as from wood.

Properties and Uses.—Methyl alcohol is a liquid of water-like appearance boiling at 64.5° and with a specific gravity of 0.812 at 0° . In its general properties it is like ethyl alcohol but is more poisonous being often fatal if taken internally. It is soluble in water in all proportions and burns with a blue non-luminous flame. It has a characteristic disagreeable odor. Because of these properties it is used as a denaturant for ordinary alcohol (p. 100). It is a good solvent of various organic substances used in manufacture and the arts, *e.g.*, shellac, and on this account is of great industrial value. It is also used in the manufacture of some synthetic dyes.

Ethyl Alcohol Ethanol Grain Alcohol



Alcoholic Fermentation.—The simple unqualified name **alcohol** applies to **ethyl alcohol** or **ethanol**. It has many important industrial uses and is of great commercial value. It is formed by the yeast fermentation of the sugar known as **glucose** or **grape sugar**. The sugar may be present as such in fruit juices or it may be the result of a preceding fermentation of some other sugar or of starch. The alcohol is obtained by distilling the fermentation liquid. Many of these fermentation liquids are used as beverages and of one kind or another are found in almost all countries. In such liquids in which the alcohol is present only in quite dilute solution the compound has been known since ancient times. It was first obtained in concentrated pure form in the middle ages, while absolute or 100 per cent alcohol was first made in 1796 and its composition determined in 1808.

Yeast.—It was known that when the juice of grapes or other sweet fruits was allowed to ferment it took on a sharp taste and affected the body in a stimulating manner. In 1836 **Cagniard de Latour** and **von Schwann** showed that alcohol was produced by the action of a living

plant organism upon sugar solutions. This organism is the common yeast plant, *Saccharomyces cerevisiæ*.

Catalytic Theory, Liebig.—Liebig held the view known as the *mechanical chemical theory* of fermentation according to which the action is due to some *catalytic* substance.

Vital Theory, Pasteur.—The views of **von Schwann** and **de Latour** were later thoroughly established by the work of **Pasteur** and it became an accepted idea that the life process of the yeast plant is directly connected with alcoholic fermentation. Yeast is able to ferment only certain ones of the common sugars, viz., **glucose** or grape sugar and **fructose** or fruit sugar. In the grape juice both of these sugars and the yeast plant also are present, the latter occurring naturally on the bloom of the grape.

Enzyme Theory, Buchner.—The recent work of **Buchner**, 1897 and later, has shown that this fermentation is due *not to the living action of the yeast cell but to a substance which he called zymase*, secreted by the cell. A number of substances originally known as ferments act catalytically in producing chemical changes of a similar nature and termed in general fermentations. **Ptyalin**, the active substance in saliva, which converts starch into sugar; **maltase**, present in intestinal juice and in malt, which converts maltose sugar into glucose; **diastase**, a constituent of malted grain, which also converts starch into maltose sugar; and **pepsin**, the active substance in gastric juice converting proteins into simpler compounds; are examples of these substances. Because alcoholic fermentation, which is the most common process of this kind, was supposed, until **Buchner's** time, to be due to a living cell, these other substances which could be obtained in a more or less pure condition were distinguished from the yeast plant ferment by the name *unorganized ferment* and later as **enzymes** the alcoholic ferment being known as an *organized ferment*.

Zymase.—**Buchner**, however, proved that the living yeast cell could be entirely destroyed and an unorganized ferment or enzyme which he called **zymase** obtained from it which in itself possessed the power of fermenting grape sugar. Thus alcoholic fermentation is of the same nature as these other fermentations and is due, like them, to the *catalytic action of an unorganized ferment or enzyme*. Thus the older views of both **Liebig** and **Pasteur** may be considered as in a way true, *i.e.*, the action as **Liebig** claimed is catalytic, depending upon the

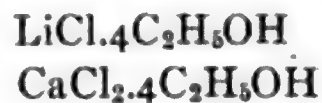
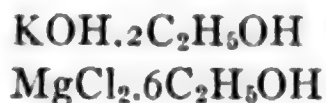
mere presence or contact of the enzyme, not upon its mass, while the living yeast cell is necessary, not directly to the fermentation itself as **Pasteur** claimed, but to the formation of the enzyme, a chemical substance which actually produces the fermentation. The alcoholic fermentation of sugar, then, is due to the action of zymase which is secreted by the yeast cell. In grapes both the sugar and enzyme are present and the juice, therefore, ferments naturally with the formation of alcohol, the resulting alcoholic liquid being known as *wine*. As wine has a considerable commercial value in itself it is not the material from which pure or high percentage alcohol is obtained.

Starch and Diastase.—The chemical substance which is the ultimate source of industrial alcohol is **starch**, or more recently **cellulose**. The material from which the starch is obtained is generally one of the cereal grains or potatoes. Starch, however, is not acted upon by the enzyme zymase so that it cannot be used directly for the alcoholic fermentation. When one of the cereal grains (or in general any starch containing seed) sprouts or begins to grow there is a gradual conversion of the starch present in the grain into sugar. - This change is brought about by the presence in the germinating grain of two enzymes, viz., **diastase** and **maltase**. The diastase converts the **starch** into a sugar known as **maltose** and maltase converts the maltose into **glucose**. When, therefore, these enzymes have acted upon the starch it is converted into a sugar upon which the alcoholic enzyme zymase can act. In practice the grain, usually corn, rye, or barley is allowed to sprout in a warm room, 60°–62°, ground, and water added making a thin mush or *mash*. This is next treated with yeast and allowed to stand at about 25°. Temperatures above 33° are injurious to the enzyme. After fermentation the mash or *wort*, as it is now called, is either placed in retorts and the alcohol distilled off directly or the liquid of the wort is separated by filtration. The amount of alcohol present in the wort is usually about 5 per cent but in wines it may go as high as 14 per cent. Above this it cannot go because a stronger solution of alcohol is destructive to the enzyme. The distillation of the alcoholic liquid takes place in a tall still, known as a *column still*, with many condensing plates so that the alcoholic vapor is continually condensed and redistilled (fractionated). By a direct distillation from such an apparatus a solution of alcohol is obtained of about 90 per cent. This may contain small amounts of the higher boiling alcohols present (**propyl** and

amyl alcohols). The non-volatile substances present in the fermentation liquid, the principal ones being **glycerol** and **succinic acid**, are left behind in the retort. For the still greater purification of the alcohol it is first mixed with water making about a 50 per cent solution. This allows the separation of some of the amyl alcohols as an oily layer. It is now distilled again through a *rectifying* or column still. By this second distillation the purest and strongest alcohol of commerce is obtained. It is about 95 *per cent* and is known as **Cologne Spirits**.

Absolute Alcohol.—For the preparation of *absolute or 100 per cent alcohol* the 95 per cent product is placed over **lime**, CaO, and after standing or heating with a return condenser to allow the lime to remove all water, the whole mass is heated and alcohol distils over as 100 per cent. **Anhydrous copper sulphate** may also be used as a dehydrating agent, but this is common only in laboratories and not in commercial practice.

Properties and Uses.—The physical and chemical properties of ethyl alcohol are similar to those of methyl alcohol, only it has a higher melting point and boiling point in accord with its relation in the homologous series. It boils at 78° and melts at -130° , specific gravity 0.806 (0°). It is a clear, water-like liquid with a pleasant pungent odor. It is poisonous in concentrated form, but in dilute condition as it occurs in beverages, it possesses stimulating effects. It burns with a blue flame. Its solvent action is similar to that of methyl alcohol though stronger toward organic substances. It also dissolves alkalies. It forms crystalline salts which contain alcohol of crystallization, *e.g.*:



Absolute alcohol, because of its affinity for water, acts as a dehydrating agent, and is used to remove the last traces of water from some substances, especially animal and plant tissues. It cannot, therefore, be kept except in bottles well stoppered.

Alcoholic Beverages

The use of alcoholic beverages is an ancient and very general custom. The natural alcoholic beverages are those weak in alcohol content and are simply the undistilled fermentation liquids. They are *wine, beer, ale, stout*, and others similar in character but with different

names. *Wine* is the simple fermented grape juice and contains between 7 per cent and 20 per cent alcohol. Those above 14 per cent are termed *fortified wines* because they have alcohol added to them. *Beer*, *ale* and *stout* are fermented liquors obtained by filtering or decanting off the fermented liquid from barley made in the general manner described in the manufacture of alcohol. These are still lower in alcohol content than wine, being between 2 per cent in *pale beers* and 5 or 6 per cent in *ales* and *porters*. The characteristic taste or flavor of wines and the names given to them depend upon the variety of grape used, the locality where the wine is made, or the particular processes involved in its manufacture. The same general facts determine the quality and name of the beers and ales. When a fermented mash prepared from grain or from fruits or molasses is distilled without attempting to secure complete purification of the distillate or the highest per cent of alcohol possible a distillate is obtained possessing certain characteristic properties due to the original material used. These liquids constitute the distilled liquors known as *whisky*, *brandy*, *cognac*, *gin*, *rum*, etc. These liquors contain from 35 per cent to 40 per cent alcohol.

Industrial Alcohol

The greatest importance of alcohol is not, however, in its use in one of these various forms as a beverage, but in its wide application in the arts as a solvent or as a substance from which other valuable compounds are made. In some of its industrial uses it may be replaced by its methyl homologue, but not in all, at least to advantage. In its synthetic uses it, of course, cannot be replaced by the other. Because of its use in beverages which are almost wholly luxuries, nearly all civilized countries have considered alcohol a proper article for taxation and for government control.

Government Regulation and Tax.—The tax is usually high so that the cost of pure alcohol is far above the cost of actual manufacture. Alcoholic beverages and high per cent alcohol that are subject to such taxation are taxed according to the amount of pure alcohol present. It, therefore, becomes necessary to determine the strength of alcoholic liquids, and also to have a fixed standard of strength.

Proof Spirit.—The standard of strength upon which alcohol is taxed is not, as might seem natural, 100 per cent or absolute alcohol,

but something less than this. In this country the standard strength is that of an alcohol-water solution of 50 *per cent, by volume*, or 42.7 *per cent, by weight*. In Great Britain it is 57.1 *per cent, by volume* or 49.3 *per cent, by weight*. This is termed *proof spirit* and tax is always made according to *per cent proof spirit*. The analysis of such liquids for alcohol *per cent* has had much attention paid to it in order to make the methods reliable and applicable to every varying condition. The general method is to take a definite amount of the liquid (100 cc.), which will be smaller the stronger the liquid, dilute to a definite volume (150 cc.) and then distil off two-thirds (100 cc.). The distillate contains the entire amount of alcohol present in the liquid and, in case necessary precautions have been taken, only water in addition. Mixtures of pure water and alcohol possess a definite specific gravity for each variation in concentration, see Table XI, so that the determination of the specific gravity of the distillate defines the exact amount of alcohol present. As this is the entire amount present in the original liquid we have an exact determination of the factor desired.

Denatured Alcohol.—Because of the high tax (U. S. tax: \$1.10 per proof gal. in 1914, \$2.20 in 1920) and, therefore, the high price of ethyl alcohol, and also because of the fact that methyl alcohol, which has no tax, cannot always be substituted for it, it is of the utmost importance that alcohol which is to be used industrially, not as a beverage, should be *removed from taxation and thus greatly cheapened in price*. Germany and England have had laws in operation for some time, removing the tax on industrial alcohol but it was not until 1906 that the United States had a law of this kind. In order to make this removal from taxation possible it is necessary to render the alcohol for industrial uses *unfit for beverage purposes*. Alcohol so treated is termed *denatured*, denaturing being accomplished by the addition of *some substance which does not interfere with the use of the alcohol industrially but makes it unfit for internal consumption*. For example, alcohol to be used in the manufacture of **ether** is denatured by the addition of **sulphuric acid** which is the reagent necessary when the ether is made. For ordinary solvent purposes the denaturant is usually **methyl alcohol**, while a little **pyridine** is often used to give it an offensive odor, and sometimes a dye is added to give a noticeable color. The denatured alcohol law has two advantages. It cheapens the cost of alcohol so that things made by its use can be likewise cheapened. It also makes it

possible to manufacture the alcohol more generally and to use in its manufacture a great many starch, sugar or cellulose containing materials which have heretofore been simply waste products of the farm. The substances generally used are fruit, most vegetables, especially potatoes, inferior grain, sawdust, etc.

TABLE XI.—ETHYL ALCOHOL

Alcohol in Per cent by Volume, Corresponding to Specific Gravity at $\frac{15.56^{\circ}}{15.56^{\circ}}$ of Mixtures of Water and Alcohol. (From Landolt's Tables, p. 226)

$d \frac{15.56^{\circ}}{15.56^{\circ}}$	Volume per cent alcohol	$d \frac{15.56^{\circ}}{15.56^{\circ}}$	Volume per cent alcohol	$d \frac{15.56^{\circ}}{15.56^{\circ}}$	Volume per cent alcohol
1.000	0	0.9709	25	0.8773	75
0.9985	1				
0.9970	2	0.9655	30	0.8639	80
0.9956	3				
0.9942	4	0.9592	35	0.8496	85
0.9928	5				
0.9915	6	0.9519	40	0.8339	90
0.9902	7			0.8306	91
0.9890	8	0.9435	45	0.8272	92
0.9878	9			0.8237	93
0.9866	10	0.9343	50	0.8201	94
0.9854	11			0.8164	95
0.9843	12	0.9242	55	0.8125	96
0.9832	13			0.8084	97
0.9821	14	0.9134	60	0.8041	98
0.9811	15			0.7995	99
		0.9021	65	0.7946	100
0.9760	20				
		0.8900	70		

Amyl Alcohols Pentanols Fusel Oil



Fusel Oil.—In the first distillation of alcohol from fermented liquids there is always present in the distillate a small amount of the higher alcohols. The mixture of these alcohols which may be separated from the ethyl alcohol is known as **fusel oil**. It contains some or all of these compounds: **propanol-1**, **butanol-1**, **2-methyl propanol-1**, **2-methyl**

propanol-2, pentanol-1, 2-methyl butanol-4, 2-methyl butanol-1, pentanol-2, 2-methyl pentanol-5, 2-methyl hexanol-6. In the manufacture of distilled liquors some fusel oil always goes over with the distillate and is contained in the liquor. It is probably this which gives to brandy and similar liquors their especially injurious effects. The fusel oil is also known as **crude amyl alcohol**, the two amyl alcohols called *active amyl*, 2-methyl butanol-1, and *inactive amyl*, 2-methyl butanol-4, being the two chief constituents. Because these two amyl alcohols are found in the fermentation liquids they are known together as **fermentation amyl alcohol**.

DERIVATIVES OF ALCOHOLS

1. ESTERS OR ETHEREAL SALTS

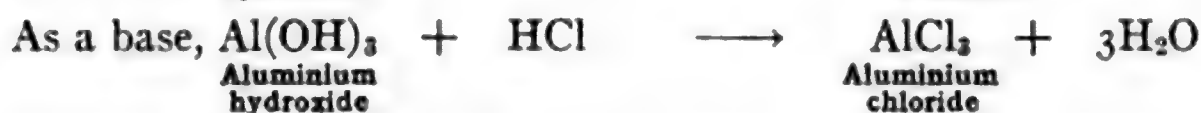


Esters or **ethereal salts** are derivatives of alcohols formed by the reaction of an **alcohol** with an **acid**. As they are thus acid derivatives also and as the more important esters are those formed from the organic acids, which we shall soon study, the chief discussion of them as a group will come later. There are, however, to be considered the esters formed from *inorganic acids* and these will be presented now. The chemical properties of alcohol in its relation to both bases and acids are of especial interest and importance. We have spoken of the fact that alcohol as an hydroxyl compound belongs to the water type, and that the other representatives of this type are the *metal hydroxides* or *bases*, and the *non-metal hydroxides* or *acids*,

Sodium hydroxide	Na—OH base
Water	H—OH neutral
Alcohol	C ₂ H ₅ —OH
Phosphorous acid	P≡(OH) ₃ acid

Now we know that while water stands as it were on the dividing line between metal and non-metal hydroxides, and is a perfectly neutral compound, there are other hydroxides which may be placed on either side, *i.e.*, they may form *either bases or acids*. The elements whose hydroxides are of this nature may be illustrated by the element **aluminium**. Toward strong bases aluminium hydroxide acts as an acid and forms salts in which the aluminium plays the part of a non-metal.

but toward strong acids it acts like a base, forming salts, of aluminium as a metal.



Alcohol a Base or an Acid.—Now alcohols are similar to aluminium hydroxide in their property of reacting with both bases and acids, as follows:

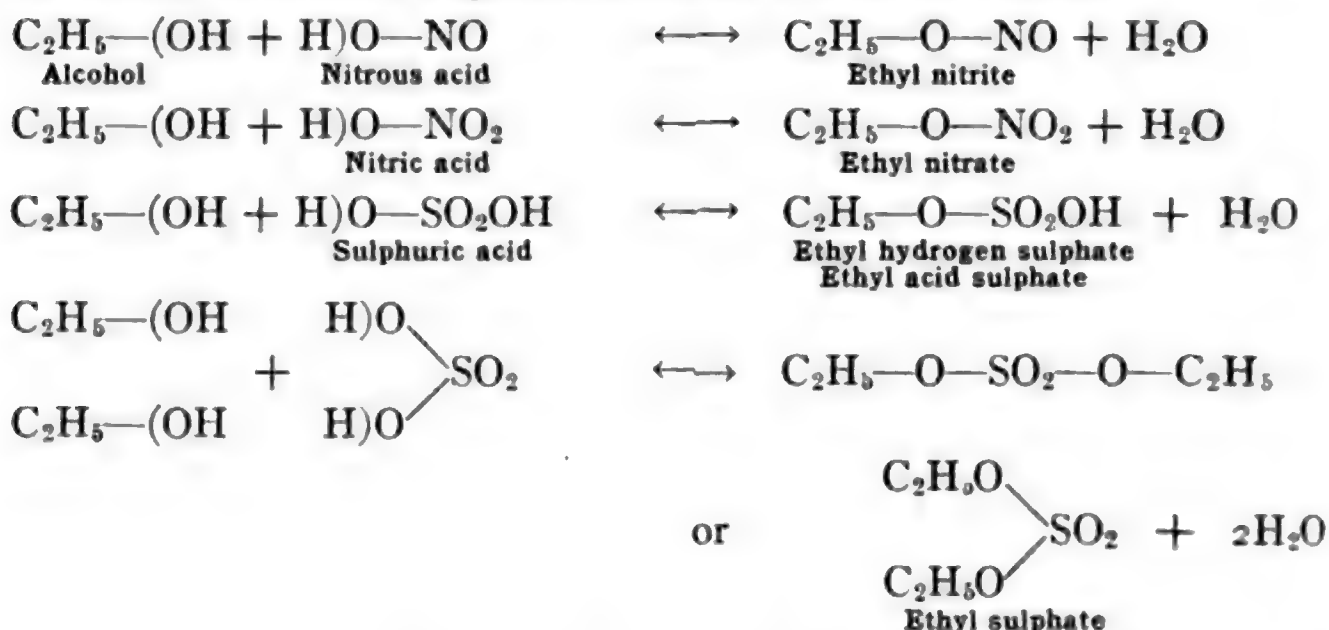


With sodium hydroxide or better with sodium, alcohol forms **sodium alcoholate**, a salt in which the ethyl radical plays the part of a non-metal, while with hydrochloric acid it forms **ethyl chloride**, a salt in which the ethyl radical plays the part of a metal. Now while alcohol acts as an acid toward only the strong bases it acts as a base toward practically all acids. We may say then that the basic character of alcohol is more pronounced than the acid. In both of these cases we have reactions that are simply the neutralization of an acid or a base by a base or an acid, the products being the same as in all neutralizations, viz., a salt and water. Both sodium alcoholate and ethyl chloride are to be looked upon then as salts.

Esters or Ethereal Salts.—The metal salts of alcohol are not of special importance, but the ethyl salts of acids are extremely important compounds. These salts in which the ethyl radical acts as a metal are called *esters* or *ethereal salts*. While the name ethereal salt is perhaps the best and most significant, as it indicates the salt character of the compound, the name *ester* will be used as it has been generally adopted. The reaction given is a general reaction of alcohols. The general formula for ester being R—(Acid R) or an alkyl radical joined to an acid radical.

In the case of the halogen acids which are binary acids or non-oxygen acids the esters are the same as the alkyl halides, *i.e.*, halogen substitution products of the hydrocarbons. With the oxygen acids, *e.g.*, nitric, sulphuric, etc., the esters are not simple substitution products of hydrocarbons. With these inorganic acids which contain oxygen the acid

radical is usually considered as that part of the acid without the hydroxyl hydrogen and the general formula for ester $R-(\text{Acid } R)$ holds. With the organic acids which also contain a hydroxyl group the acid radical does not include the hydroxyl oxygen and the general formula for such esters becomes $R-O-(\text{Acid } R)$. This will be made clear later. With ethyl alcohol again as our illustration, the esters of nitrous, nitric and sulphuric acids are formed as follows:



As sulphuric acid is *dibasic* it forms two kinds of esters, one *acid* and one *neutral*. These are analogous to the acid and neutral salts that are formed when sulphuric acid is neutralized with sodium hydroxide. In the same way alcohols form *mono*-, *di*- and *tri-alkyl esters* with **phosphoric acid** analogous to the *mono*-, *di*-, and *tri-basic salts* of sodium and phosphoric acid. The *esters of nitrous acid* are isomeric with the *nitro substitution products* of the hydrocarbons (p. 74). The two classes of compounds are, however, distinctly different. The *nitro compounds* formed by the reaction between an *alkyl halide and silver nitrite*, have the nitro group ($-\text{NO}_2$) substituted for a hydrogen of the hydrocarbon, *e.g.*, $\text{C}_2\text{H}_5-\text{NO}_2$. In these the *nitrogen is linked directly to the carbon* as shown by their reduction to *amino compounds*. On the other hand, the isomeric *nitrous acid esters* are formed by the reaction given above between an *alcohol and nitrous acid*. In these esters the group ($-\text{O}-\text{NO}$) replaces the hydroxyl of the alcohol and the *union of the nitrogen is not directly with the carbon but through an intervening oxygen atom*, $\text{C}_2\text{H}_5-\text{O}-\text{NO}$. Furthermore the esters are *easily decomposed by water yielding the alcohol* while the nitro compounds are *not* thus decomposed by water.

Properties.—This easy decomposition by water, especially in the presence of alkalies, is a characteristic property of esters. Because of this fact the reaction for the formation of an ester reverses when the concentration of the water, which is the other product of the reaction, becomes strong enough. The reaction is therefore written *with double arrows to indicate its reversible nature*. When such reversal of the reaction occurs the alcohol is again formed. This was mentioned in connection with the synthesis of alcohols from alkyl halides (p. 92). The first part of the name, ethereal salt, is derived from their general character as more or less volatile and pleasant smelling substances. This applies especially to the esters formed with the organic acids which we shall soon consider. It is also among these esters of the organic acids that we find the most important representatives of the group and those which are found most widely distributed in plants and animals.

2. ETHERS R—O—R

The importance of the esters of ethyl alcohol and sulphuric acid is in connection with the formation of the compounds we shall now take up, viz., *ethers*.

Synthesis.—The salts of strong metals with alcohols we have shown are represented as $\text{CH}_3\text{—ONa}$, $\text{C}_2\text{H}_5\text{—ONa}$, etc. When an alkyl halide acts upon these compounds one of the products is a substance known as an *ether*, the other product is the sodium halide. The reaction must be then, in the case of ethyl alcohol:



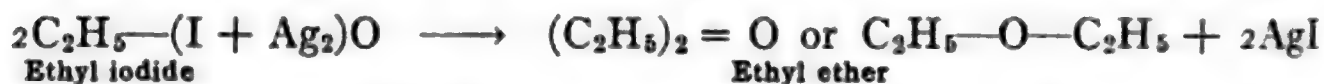
Williamson's Synthesis.—This reaction is known as **Williamson's synthesis** because, in 1851, he showed, by it, the true constitution of ether, and made possible the explanation of its preparation from alcohol and sulphuric acid as given a little later on. The reaction is similar to the **Wurtz** reaction between sodium and an alkyl halide by which a hydrocarbon is formed.



The constitution of ether seems to be well established simply by this one reaction which in general is



A second synthesis of ethers proves again that their constitution is that of an oxide of an alkyl radical. When an alkyl halide is heated with dry silver oxide, Ag_2O , an ether is formed:



As alcohols have been shown to be *hydroxides* so the ethers, by these syntheses, are *oxides*, for the sodium which in sodium ethylate has replaced the hydroxyl hydrogen of the alcohol is, in ether, replaced by a second alkyl radical. The following formulas may make these relationships plain.

Sodium hydroxide	Na—O—H	Na—O—Na	Sodium oxide
Alcohol	$\text{C}_2\text{H}_5\text{—O—H}$	$\text{C}_2\text{H}_5\text{—O—C}_2\text{H}_5$	Ethyl ether
(ethyl hydroxide)			(ethyl oxide)

Simple Ethers and Mixed Ethers

Just as there is an homologous series of alcohols so there is also an homologous series of ethers, each alcohol having a corresponding ether. Thus we have **methyl ether**, $\text{CH}_3\text{—O—CH}_3$, **propyl ether**, $\text{C}_3\text{H}_7\text{—O—C}_3\text{H}_7$, etc. As by the **Wurtz synthesis** of hydrocarbons we can theoretically unite any radical with any other radical by heating the iodide of one with the iodide of the second in the presence of sodium, so by the **Williamson synthesis** we should be able to form ethers by uniting any radical with any other radical through the oxygen of the sodium alcoholate. The formula for ethers then, R—O—R , may be written R—O—R' , in which *R* and *R'* may be the *same* or may be *different*. Ethers in which they are the same are called *simple ethers*, and when they are different the ethers are called *mixed ethers*.

Names of Ethers.—The systematic official names of ethers are made by using the term *oxy* in connection with the hydrocarbon names corresponding to the alkyl radicals. The common names are the same as the alcohols with ether in place of alcohol. The following table gives some of the better known ethers of both kinds and will illustrate the nomenclature.

Isomerism.—The isomerism of the ethers may be due to several things. Referring to Table XII we see that in simple ethers it may be due to isomerism of the alkyl radicals as in **propyl ether** and in **isopropyl ether**. In mixed ethers two different sets of alkyl radicals yield

someric ethers as in **methane-oxy-1-propane** and **methane-oxy-2-propane**. Also a mixed ether may be isomeric with a simple ether as **methane-oxy-propane** and **ethane-oxy-ethane** or **propane-oxy-propane** and **propane-1-oxy-2-propane**.

Class Isomerism.—We have also with the ethers a new case of isomerism different from any we have studied. It will be seen on examining the empirical formulas of ethers that they are the same as the alcohols with an equal number of carbon atoms.

C_2H_6O **Methyl ether**, CH_3-O-CH_3 **Ethyl alcohol**, C_2H_5-OH
 $C_4H_{10}O$ **Ethyl ether**, $C_2H_5-O-C_2H_5$ **Butyl alcohol**, C_4H_9-OH

Here isomerism is not due to difference in structure in compounds of the same class but to *difference in the class to which compounds of the same composition belong*. Such isomerism may be called *class isomerism* and is a form of structural isomerism.

Chemical Properties.—Chemically the ethers are not very active nor do they lead to important derivatives. Chlorine forms substitution products in which, as in methyl ether, one to six hydrogens of the alkyl radicals are substituted. The halogen acids, especially hydriodic acid, form an alcohol by a reaction analogous to the reversion of the **Williamson synthesis**.



Ethyl Ether $C_2H_5-O-C_2H_5$ **Ethane-oxy-Ethane**

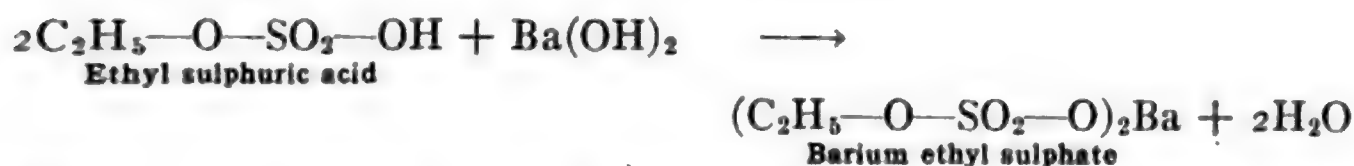
The most important ether of the whole group is **ethyl ether** which is the common ether of commerce, the formula of which is $C_2H_5-O-C_2H_5$. This ether may be prepared by either of the syntheses given above. These are not, however, the methods used in preparing it on the large scale. The commercial process is as follows:

Commercial Manufacture.—Alcohol and sulphuric acid are mixed in the proportion of *one molecule of alcohol to one molecule of sulphuric acid*. This is in the proportion of 46 grams alcohol (molecular mass of alcohol equals 46) to 98 grams sulphuric acid (molecular mass equals 98) or approximately one part alcohol (absolute) by weight to two parts sulphuric acid (concentrated) by weight. This will be found to be approximately in the proportion of one volume alcohol to one volume sulphuric acid. After cooling the well shaken mixture it is

heated to 140° and when this temperature is reached fresh *alcohol is added slowly* through a tube reaching below the surface of the mixture. As alcohol is added ether distils over, and *as long as fresh alcohol is added ether is formed*, in an amount equivalent to the alcohol added, *two molecules of alcohol yielding one molecule of ether*. This operation may be continued indefinitely. The explanation of this reaction was first made clear by **Williamson** and is as follows: When alcohol and sulphuric acid react, in the proportion of one molecule of each, **ethyl sulphuric acid** is formed.



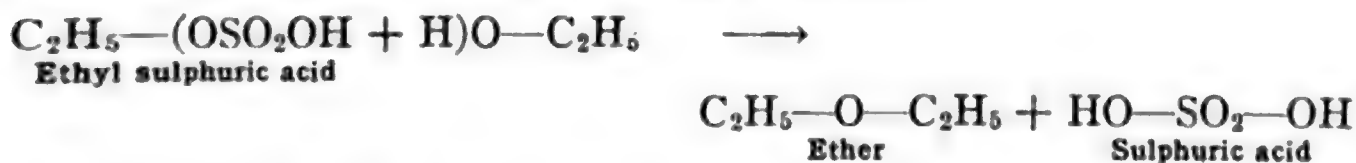
This may be isolated as an easily soluble crystalline compound, also in the form of its barium or calcium salts by neutralizing the remaining acid hydrogen with barium or calcium hydroxide.



When ethyl sulphuric acid is boiled with water it acts as do esters in general. The reaction of its formation is reversed and alcohol and sulphuric acid are reformed.



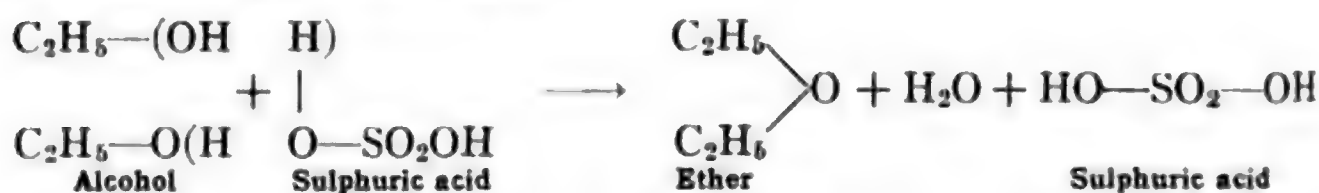
Now in the first stage of the preparation of ether, **ethyl sulphuric acid** is formed. When this is heated to 140° and fresh alcohol is added the reaction is analogous to that between ethyl sulphuric acid and water, **ether** is formed and **sulphuric acid** is *regenerated*.



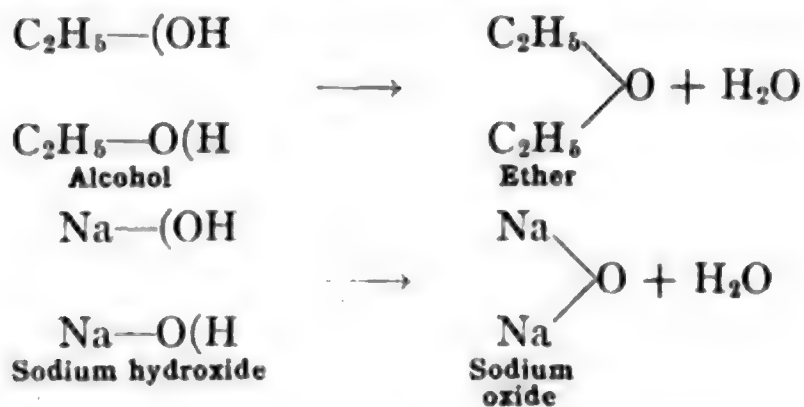
This sulphuric acid then unites with more alcohol forming ethyl sulphuric acid which again reacts with alcohol and yields ether and sulphuric acid. Thus the sulphuric acid remains in the reaction mixture either as ethyl sulphuric acid or as free sulphuric acid. It acts as a carrier of the ethyl radical or it is perhaps better to say as a dehydrating agent removing the water which is the other product of the first step in the reaction. We have said that the reaction goes on indefinitely.

This is not strictly true because the water formed, though partly removed by distillation, gradually dilutes the acid until it is too weak to react with the alcohol, *i.e.*, until the reversible reaction occurs and the ethyl sulphuric acid, as fast as it is formed, is decomposed again into alcohol and sulphuric acid. Also the heat of the reaction gradually uses up the acid owing to its reduction by means of the alcohol.

Ether the Anhydride of Alcohol.—On examination of the double reaction it is seen that, in effect, the result has been to *remove one molecule of water from two molecules of alcohol*. The hydroxyl is taken from one alcohol molecule and the hydrogen from the other. We may represent the combined reaction as one.



In fact, of course, the hydrogen from the second molecule of alcohol goes to re-form sulphuric acid, but as it simply replaces the hydrogen given by the acid to form water with the alcoholic hydroxyl of the first molecule of alcohol the result is in effect as we have stated. This means then that ether is the *anhydride of alcohol* and their relation to each other is analogous to that between metal and non-metal hydroxides and oxides.



This agrees with the constitution of ether as established by its synthesis from sodium ethylate and ethyl iodide, **Williamson's synthesis**, or from ethyl iodide and silver oxide (p. 106).

Properties of Ether.—Ethyl ether is the common ether used so generally as an anesthetic and is one of the most valuable of the substances made from alcohol. In its manufacture denatured alcohol is an important factor. The reason why the denaturing of the alcohol by the addition of sulphuric acid does not injure the alcohol for this purpose is apparent. Ether is a clear, limpid liquid of characteristic odor

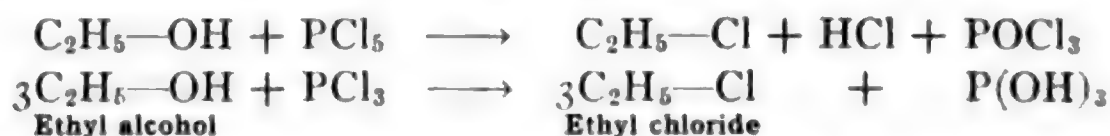
and is easily volatile, boiling at 34.6° . It burns and is very inflammable because it is so volatile. The vapor forms an explosive mixture with air, and it is, therefore, extremely dangerous to use unless great precaution is taken to guard it from ignition. It does not dissolve in water except in small amounts, and as it is lighter than water, specific gravity 0.736 (0°) it forms a non-miscible layer on top of the water whenever the two are mixed and then allowed to stand and separate. This property is made use of very often in separating ether and water and in extracting from water solution substances which are more soluble in ether. It mixes with alcohol in all proportions. It is a good solvent for many organic substances, fats and alkaloids especially. Because of its rapid evaporation at ordinary temperatures it lowers the temperature of a body sprayed with it.

III. OXIDATION PRODUCTS OF ALCOHOLS



Oxidation of Alcohol.—When ethyl alcohol is treated with potassium bichromate in the presence of dilute sulphuric acid a volatile substance with a peculiar sweet odor is given off. At the same time the reduction of the bichromate is indicated by the appearance of the green color characteristic of chromium salts. The volatile product is termed an **aldehyde**, specifically **acetaldehyde**, and when analyzed proves to have the composition, $\text{C}_2\text{H}_4\text{O}$. As this differs from the alcohol by two hydrogen atoms the action has plainly been one of oxidation by which two hydrogen atoms have been removed. The name is derived from this relation to alcohol, from the two words *al-(cohol) dehyd-(rogenatum)*.

Aldehydes not Hydroxy Compounds.—The question arises, which two hydrogen atoms of the alcohol have been removed and what is the constitution of the new compound? Alcohol is $\text{C}_2\text{H}_5\text{—OH}$ or $\text{CH}_3\text{—CH}_2\text{—OH}$ so that we might lose two hydrogen atoms in various ways. The first test that naturally suggests itself is to determine whether the aldehyde still contains the hydroxyl group of the alcohol or is this hydroxyl hydrogen one of those removed? When treated with metallic sodium acetaldehyde forms no compound nor does it lose one hydrogen as in the case of alcohol. This would indicate that in aldehydes *no one atom of hydrogen differs from the others, i.e., all must be directly linked to carbon and no hydroxyl group is present*. In proving the constitution of alcohol as a hydroxy compound (p. 80) the reaction with **phosphorus tri- and penta-chlorides** established it as analogous to that of water. The reactions are as follows:

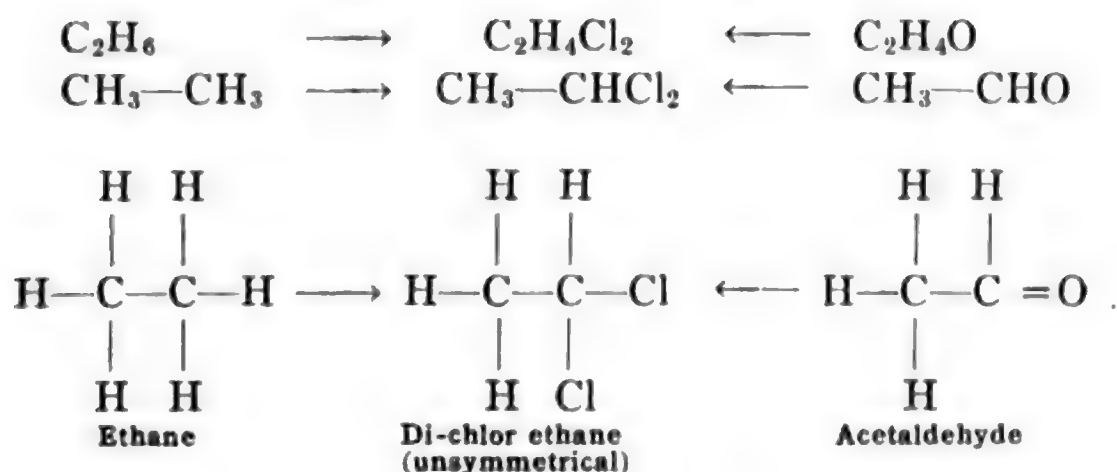


With acetaldehyde and phosphorus penta-chloride the products of the reaction are entirely different. There is *no formation of either hydro-*

chloric acid or an alkyl chloride. This proves that in aldehyde there can be *no hydroxyl group* as the formation of these two products, especially the hydrochloric acid, is proof of the existence of this group. The products formed are **phosphorus oxy-chloride**, POCl_3 , and a compound which by analysis proves to be $\text{C}_2\text{H}_4\text{Cl}_2$.



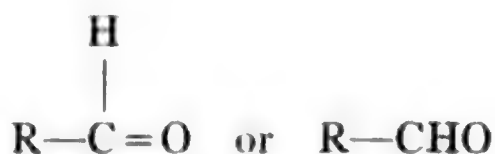
Plainly the reaction here is the same as that given as the probable first step in the action of phosphorus penta-chloride and alcohol, viz., two atoms of chlorine of the penta-chloride have been exchanged for oxygen yielding phosphorus oxy-chloride, POCl_3 . The other product in the aldehyde reaction has been shown to be ethane in which two hydrogen atoms are substituted by two chlorine atoms, *i.e.*, a *di-chlor ethane*. Furthermore, *the* di-chlor ethane so formed is the *unsymmetrical* compound (p. 53), in which *two hydrogen atoms linked to one carbon* have been substituted by two chlorine atoms. It must be then that in acetaldehyde *one atom of oxygen is in the position of two atoms of hydrogen linked to one carbon in ethane*. These relations, between **ethane**, **unsymmetrical di-chlor ethane** and **acetaldehyde** may be represented as follows:



Aldehydes, then, *are not hydroxy compounds* nor are they oxides like the ethers. In them the *oxygen atom is linked to one carbon atom by two valencies* previously satisfied by two hydrogen atoms in the hydro-carbon mother substance.

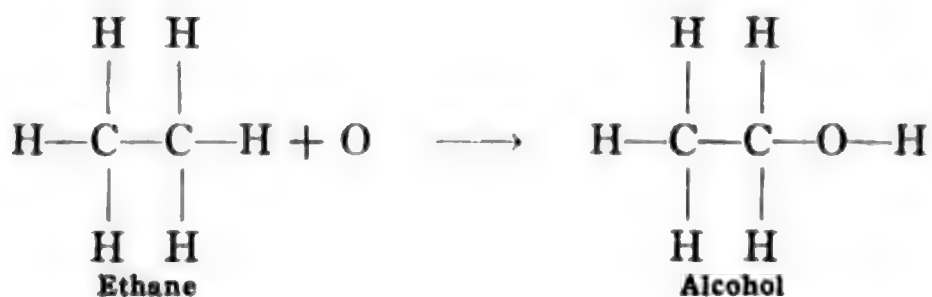
Carbonyl Group.—This group, viz., $=C=O$ is known as *carbonyl* and it is present in other compounds also. The other two valencies of the carbon to which the oxygen is linked are satisfied in acetaldehyde, one by hydrogen, the other by methyl.

Aldehyde Group.—This methyl may become any radical thereby forming an homologous series of aldehydes. The hydrogen, however, remains in all aldehydes so that the distinctive aldehyde formula is



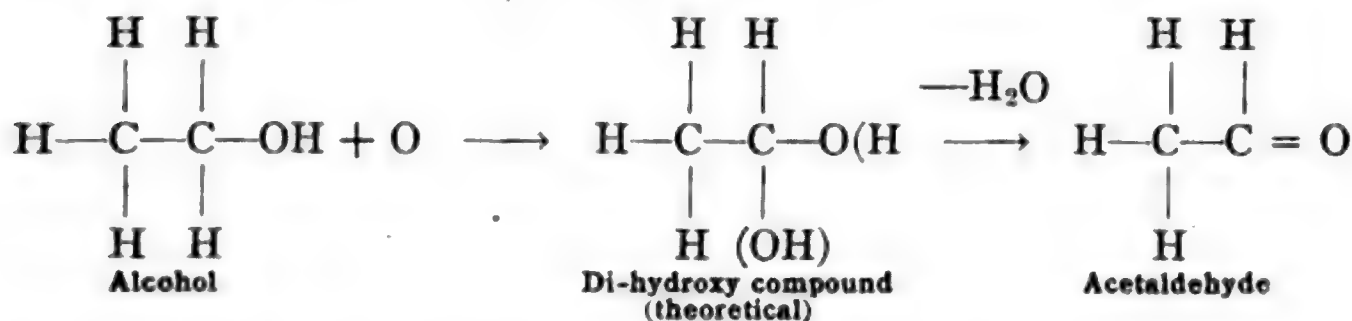
It will be well to note that in writing formulas in the condensed structural form, $\begin{array}{c} | \\ -\text{COH} \end{array}$ indicates that *hydroxyl is linked to carbon* while $\begin{array}{c} | \\ -\text{CHO} \end{array}$ indicates that *hydrogen and oxygen are linked separately to the carbon*.

Alcohol an Oxidized Hydrocarbon.—Our first statement in regard to acetaldehyde was that it is formed by oxidizing alcohol. This reaction, and the further oxidation of aldehydes to acids, which we shall study very soon, are only clear when we consider alcohols as the first step in the oxidation of hydrocarbons. We cannot prepare ethyl alcohol by oxidizing ethane, and we have shown that it is not an oxide, but in composition it is plainly an oxidation product, *i.e.*, ethane plus oxygen. We can consider it as such in that a *hydrogen atom of ethane is converted into hydroxyl by the addition of oxygen, the oxygen forming the link between carbon and hydrogen*. We may represent the relationship as follows:

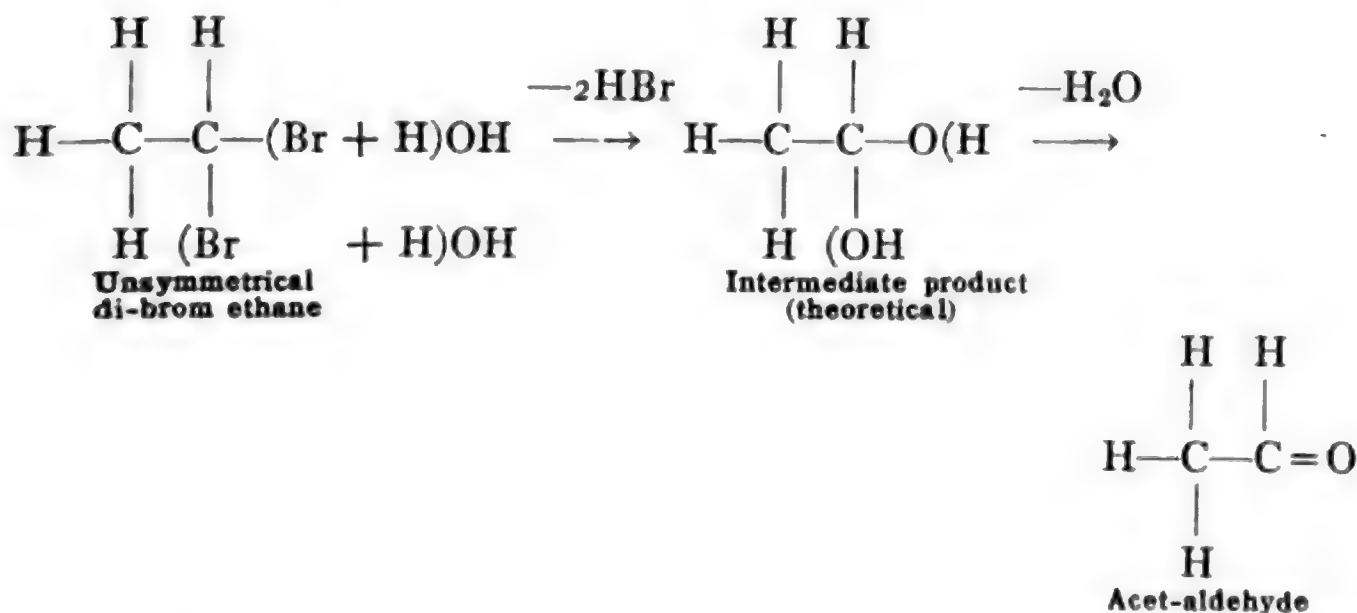


If this is the process in the oxidation of compounds containing hydrogen linked to carbon we should expect a second oxygen to react in the same

way and a di-hydroyl compound would be formed. But we know that when alcohol is oxidized we obtain an aldehyde which we have shown has the constitution previously assigned to it. On examination we see that this formula for the aldehyde is simply the anhydride of the theoretical oxidation product represented as an intermediate step in the oxidation of alcohol to acetaldehyde, as follows:



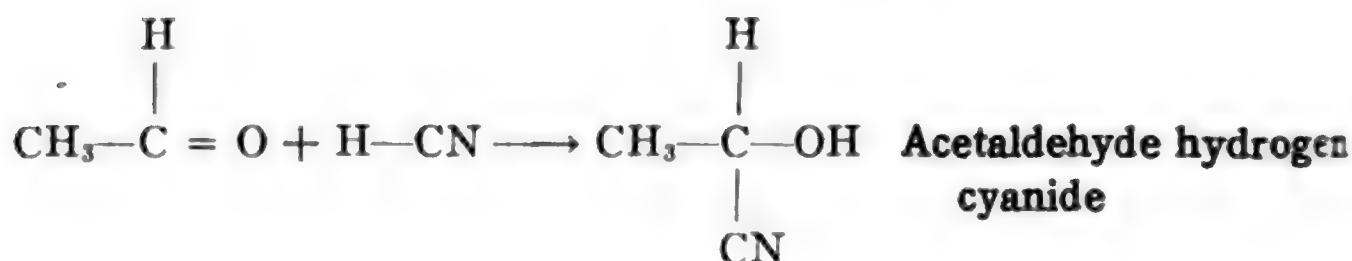
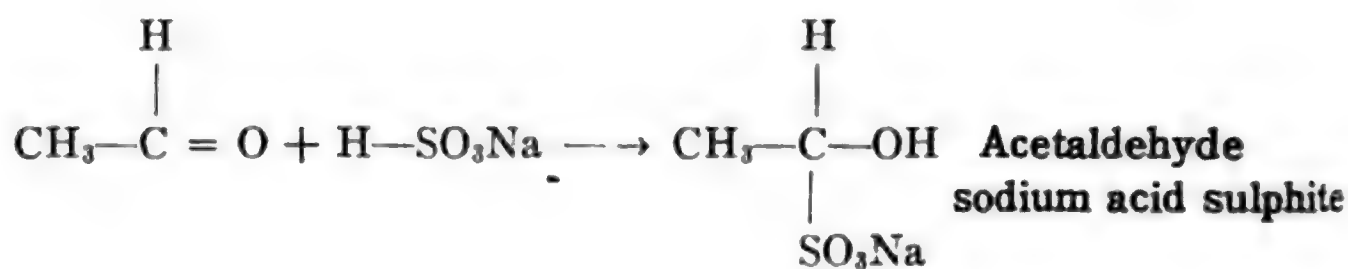
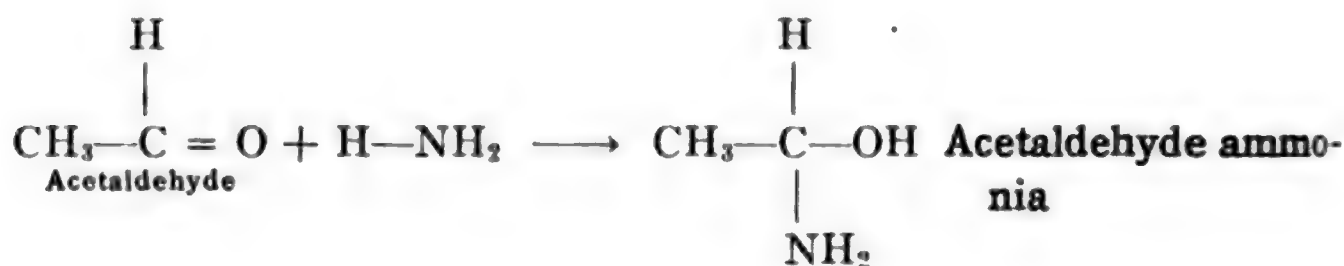
It should also be emphasized that when oxidation of an hydroxy compound takes place the carbon group that is oxidized is one which already contains hydroxyl. This formation of a di-hydroxy compound as an intermediate product in the oxidation of alcohol to an aldehyde may also be shown to be the probable step by the fact that acetaldehyde may be made from **unsymmetrical di-brom ethane** by the action of water as follows:



Two Hydroxyls Linked to One Carbon.—Now a great many cases have led to the conclusion that whenever we have *two hydroxyls linked to one carbon* an *unstable grouping* is the result. This loses water as indicated and a stable anhydride product is formed. We shall find

later that when *two hydroxyls are linked to two different carbons a stable compound* is formed which does not lose water.

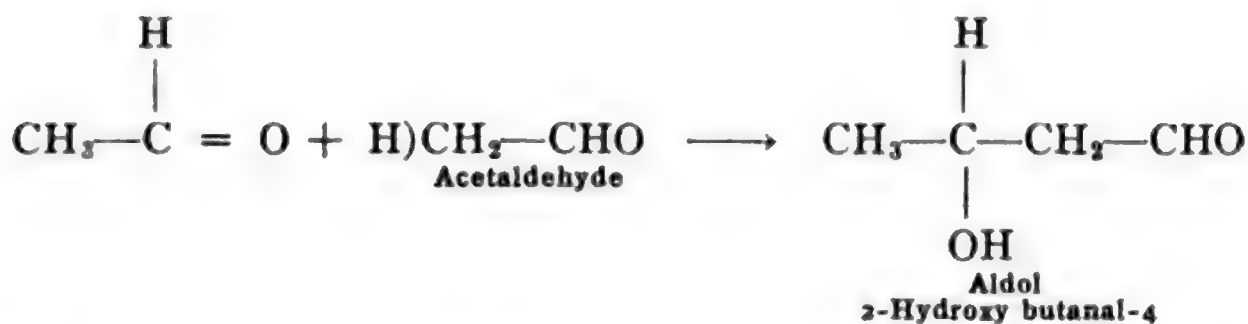
.Addition Products.—An important property of aldehydes is that they readily take up certain compounds and form *addition products*. When acetaldehyde reacts with **ammonia**, **sodium acid sulphite** or **hydrogen cyanide** definite crystalline compounds are obtained. The probable reaction is that the double union between carbon and oxygen is broken the oxygen being converted into hydroxyl, while the remainder of the added compound satisfies the other valence as follows:



The probability that these are the formulas for the addition products is based upon the fact that the formula for the hydrogen cyanide compound is fully established by its relationship to another definite compound, viz., **lactic acid**, on account of which it is known as **lactic acid nitrile**. This will be explained later when we study that acid.

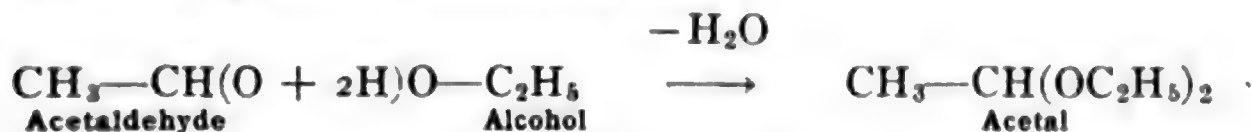
Aldol Condensation.—An important reaction of acetaldehyde, which is analogous to the preceding addition reactions, is one in which a molecule of acetaldehyde forms an addition product with itself, the two molecules being united into one. The reaction is designated a *con-*

condensation and from the name of the product it is termed the **aldol condensation**.



Aldol is a hydroxyl substitution product of normal butyric aldehyde or butanal. This reaction and the product will be referred to later (p. 229).

Acetal.—Under certain conditions, by passing phosphine gas, PH_3 , into a mixture of alcohol and acetaldehyde, the two compounds react yielding a product known as **acetal**.



Acetal may also be made by oxidizing alcohol when the above reaction probably takes place. It is present too in crude wood distillate from which it may be obtained.

Polymerization.—Another property of aldehydes that should be mentioned is that some of them readily form *polymeric compounds*, *i.e.*, compounds of the same percentage composition, but some multiple of the molecular weight.



This polymeric aldehyde, known as **par-aldehyde**, is a definite compound, but it does not react like an aldehyde, *i.e.*, does not contain the aldehyde group. The polymerization is effected by simply adding a small amount of acid. Furthermore, at 0° , the same reaction takes place, but a distinctly different product is obtained which proves to be a similar polymeric compound of the same formula as the paraldehyde. This is known as **met-aldehyde**. A comparison of these two compounds shows their difference.

Paraldehyde
($\text{C}_2\text{H}_4\text{O}$)₃

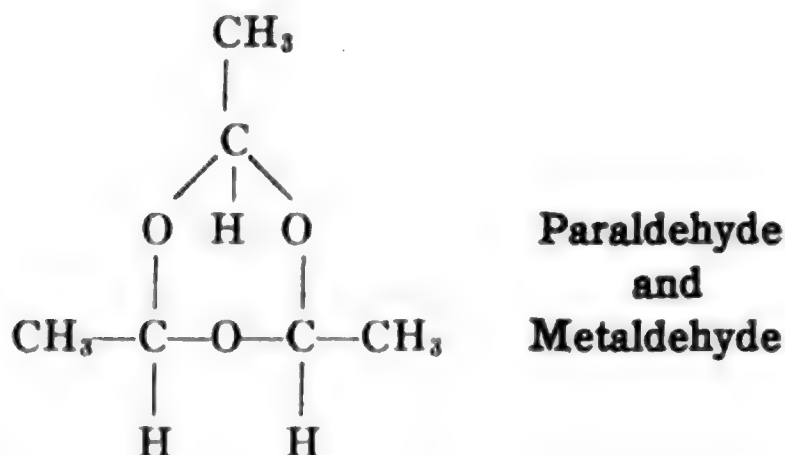
Acetaldehyde + HCl
Liquid, B.P. 125°

Metaldehyde
($\text{C}_2\text{H}_4\text{O}$)₃

Acetaldehyde + HCl at 0°
Solid, sublimes at 112°

By such polymerization then two isomeric compounds are formed *neither of which contains the aldehyde group*.

The loss of aldehyde properties by a change in the aldehyde group is due to the union of the three molecules into a ring. The isomerism of the two polymers is probably due to different space relations, *i.e.* it is *stereo-isomerism*. The following formula has been suggested.



Reducing Properties.—The ease with which aldehydes are oxidized makes them important as reducing agents. When acetaldehyde or the ammonium acetaldehyde acts upon silver nitrate in ammoniacal solution the silver is reduced to metallic condition. The metallic silver so formed is in an exceeding fine condition and is deposited as a brilliant mirror on the clean surface of the glass vessel in which the reaction occurs.

Nomenclature.—While there is an homologous series of aldehydes as of the other compounds we have studied, only a few of them are important. The official names correspond exactly to those for the alcohols, the termination *ol* of alcohols being changed to *al* for the aldehydes. The first four members are **methanal**, **ethanal**, **propanal**, **butanal**. The common names are derived from the fact that aldehydes *on further oxidation yield acids*, the name of the acid resulting giving the specific name to the aldehyde. **Formic acid** is obtained from **formic aldehyde**, contracted to **formaldehyde**; **acetic acid** from **acetic aldehyde**, **acetaldehyde**. Those two aldehydes are the most common and the only ones we shall consider. The aldehydes have in general lower boiling points than the corresponding alcohols and a peculiar, irritating sweet odor. Table XIII gives the names, formulas and boiling points of a few aldehydes.

TABLE XIII.—ALDEHYDES AND KETONES
Aldehydes

Common name	Official name	Formula	B.P.
Formaldehyde.....	Methanal.....	H—CHO	−21°
Acetaldehyde.....	Ethanal.....	CH ₃ —CHO	20.8°
Propionic aldehyde.....	Propanal.....	CH ₃ —CH ₂ —CHO	48.8°
Butyric aldehyde.....	Butanal.....	CH ₃ —CH ₂ —CH ₂ —CHO ?	74.0°
Iso-butyric aldehyde.....	2-Methyl propanal.....	CH ₃ —CH—CHO ? CH ₃	61.0°
Valeric aldehyde.....	Pentanal.....	CH ₃ —CH ₂ —CH ₂ —CH ₂ —CHO	103.4°
Iso-valeric aldehyde.....	2-Methyl butanal-4.....	CH ₃ —CH—CH ₂ —CHO CH ₃	92.0°

Ketones

Acetone (Di-methyl ketone).....	Propanone.....	CH ₃ —CO—CH ₃	56.5°
Methyl ethyl ketone.....	Butanone.....	CH ₃ —CO—CH ₂ —CH ₃	80.6°
Di-ethyl ketone.....	Pentanone-3.....	CH ₃ —CH ₂ —CO—CH ₂ —CH ₃	102.0°
Methyl propyl ketone.....	Pentanone-2.....	CH ₃ —CH ₂ —CH ₂ —CO—CH ₃	102.7°
Methyl iso-propyl ketone..	2-Methyl butanone-3.....	CH ₃ —CH—CO—CH ₃ CH ₃	95.0°
Methyl nonyl ketone.....	Undecanone-2.....	CH ₃ —CO—(CH ₂) ₈ —CH ₃	224.0° M.P. +15°

Formaldehyde H—CHO. Methanal

Formaldehyde or *methanal* is the aldehyde related to methyl alcohol as the oxidation product. It may be prepared by passing a mixture of methyl alcohol vapor and air over hot copper or platinum.



The reaction continues after being started because the heat of the reaction keeps the metal hot. It is a gas, b.p. −21°, and is readily soluble in water. A solution containing about 40 per cent is the commercial form of the compound known as *formalin* sometimes also as *formol*. Formaldehyde is a valuable preservative, antiseptic and germicide, and is used widely in disinfecting, either as a gas or in the form of a water solution, viz., as formalin. When formalin is used it is sprinkled upon a sheet which is suspended in the room, the formalde-

hyde volatilizing as a gas. When used in the form of a gas, as in disinfecting rooms after sickness, it is freshly generated by means of alcohol lamps so constructed with platinum asbestos that the reaction above described takes place. A still more effective way is by the action of potassium permanganate upon formalin. When formalin is poured upon potassium permanganate a vigorous action occurs with the production of much heat so that the greater part of the formaldehyde is volatilized. The action is quite violent and the gas is driven rapidly throughout the entire space to be disinfected.

Acetaldehyde $\text{CH}_3\text{—CHO}$. Ethanal

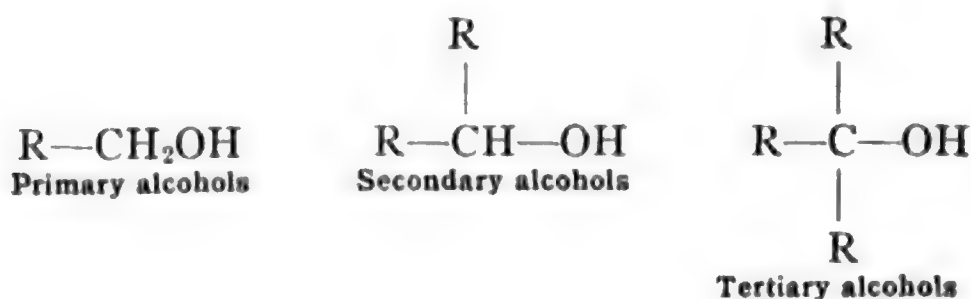
Acetaldehyde or *ethanal* is the second member of the series and corresponds to ethyl alcohol from which it is made by oxidizing with chromic acid (potassium bichromate and sulphuric acid).



The name ethanal indicates its relation to ethyl alcohol while, as it forms acetic acid on further oxidation, it is known also as acetaldehyde. It is a volatile liquid boiling at 20.8° , and possessing a sharp sweet odor. It is soluble in water, alcohol, and ether.



Ketones are also oxidation products of alcohols. We should recall that there are three different kinds of alcohols isomeric because of the different places in the hydrocarbon chain in which the hydroxyl is substituted. These alcohols we have called *primary*, *secondary* and *tertiary*, and each one contains a characteristic group, viz.,



Primary Alcohols Yield Aldehydes.—Now methyl alcohol and ethyl alcohol which yield the two aldehydes that have been studied are both of them primary alcohols, and it has been found to be true that *only primary alcohols yield aldehydes on oxidation*. Normal propyl alcohol, propanol-1, and other primary alcohols thus yield aldehydes.

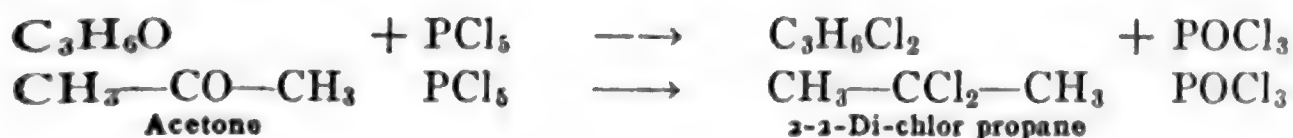


Secondary Alcohols Yield Ketones.—The isomeric propyl alcohol, viz., the *secondary alcohol*, **propanol-2**, on oxidation yields a compound the composition of which is $\text{C}_3\text{H}_6\text{O}$, but which is *not* an aldehyde. It is known as a *ketone*, specifically as **acetone**, and is isomeric with **propanal** the aldehyde obtained from normal propyl alcohol.



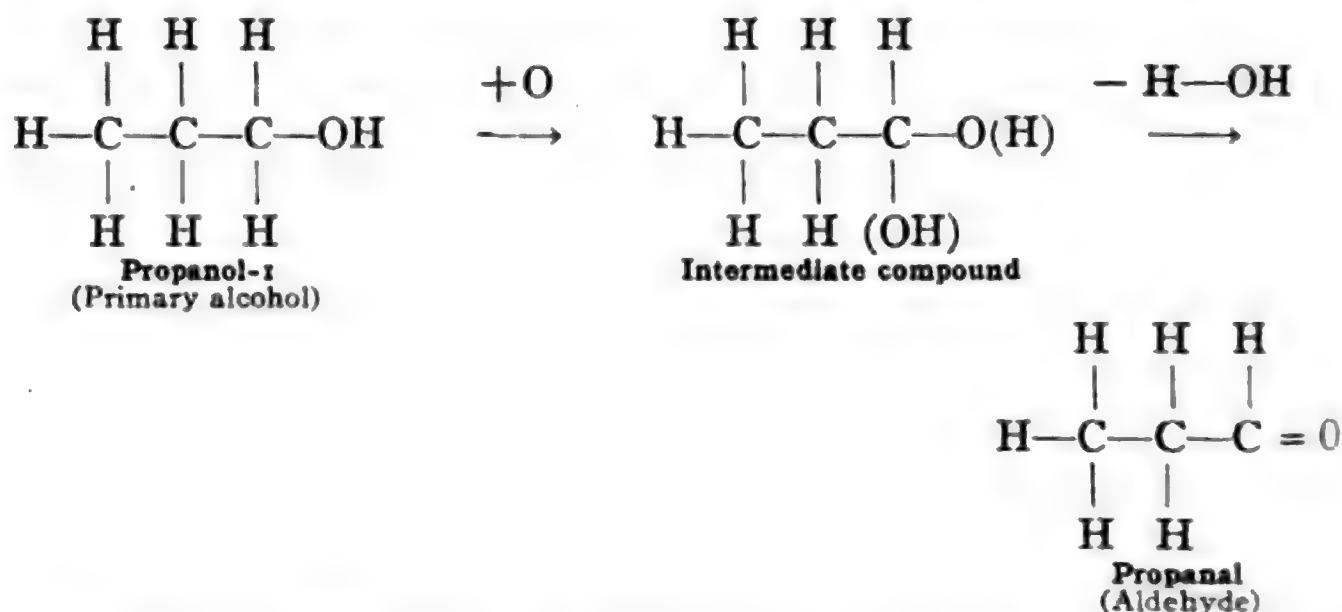
As only those alcohols which are *primary* yield *aldehydes* so also only those which are *secondary* yield *ketones*. The relation in composition between the secondary propyl alcohol and acetone is the same as between ethyl alcohol and acetaldehyde. What then is the constitution of ketones and why do secondary alcohols not oxidize to aldehydes but to ketones?

Action of PCl_5 on Ketones.—When **phosphorus penta-chloride** reacts with **acetone** it acts just as it does with aldehydes, *i.e.*, it removes oxygen and substitutes two chlorine atoms in its place. The product is **2-2-di-chlor propane**.

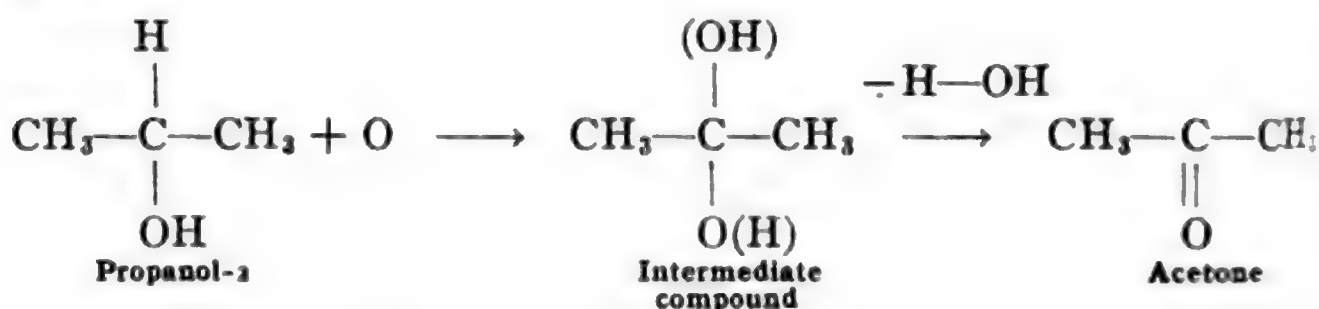


Carbonyl Group in Ketones.—This reaction would indicate the presence of the *carbonyl group*, ($=\text{CO}$), and the structure as written. Now acetone by reduction yields **propanol-2** and conversely is formed from it by oxidation. Propanol-2 is $\text{CH}_3\text{—CH(OH)—CH}_3$, *i.e.*, there are *two methyl groups* present. Do these two methyl groups, however, remain in acetone as they exist in the alcohol? We have stated previously (p. 115) that the oxidation of primary alcohols probably takes

place by the conversion of a hydrogen into a second hydroxyl group and that this product loses water and gives us aldehyde as follows:



Structure of Ketones.—If **propanol-2** is oxidized in the same way we should obtain an intermediate product containing *two* hydroxyl groups linked to one carbon atom and this would lose a molecule of water as follows:



The conclusive proof that in acetone there are two methyl groups present is in the synthesis of **acetone** from **acetic acid** and **acetyl chloride**, reactions which we shall soon study. With this conclusive proof our formula, as we have written it, must be correct and our ideas in regard to the oxidation of compounds containing hydrogen linked to carbon are probably correct also. The steps in the oxidation are probably as we have indicated, viz., that *hydrogen is first converted into hydroxyl* and when as a result of such oxidation, *two hydroxyls are linked to one carbon*, the compound *loses water*, leaving *one oxygen doubly linked to the carbon*. This enables us to understand the facts that *only primary alcohols on oxidation yield aldehydes*, *secondary alcohols yield ketones*, while *tertiary alcohols yield neither aldehydes nor ketones*.

Oxidation of Primary Alcohols.—In the *primary alcohol* group ($-\text{CH}_2\text{OH}$), there are *two* unoxidized hydrogens.

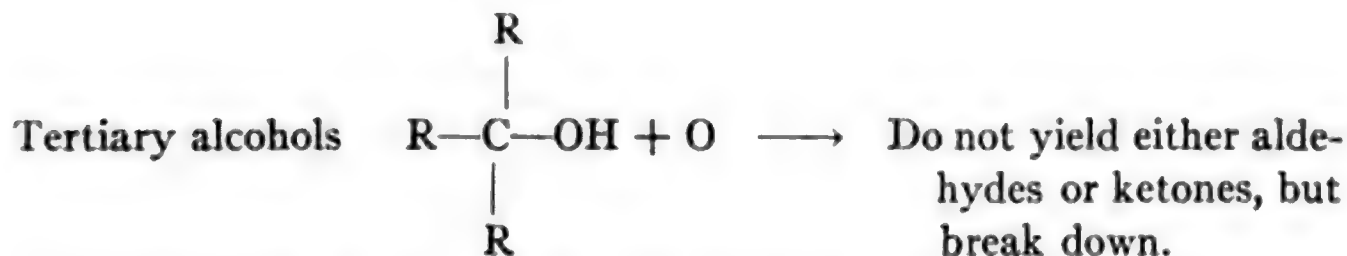
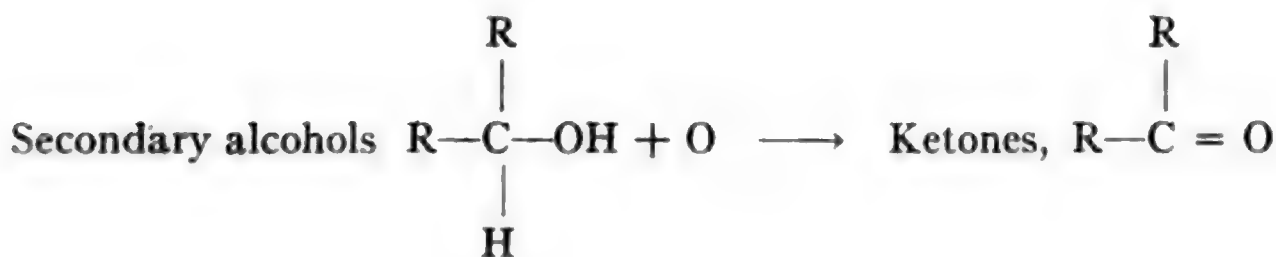
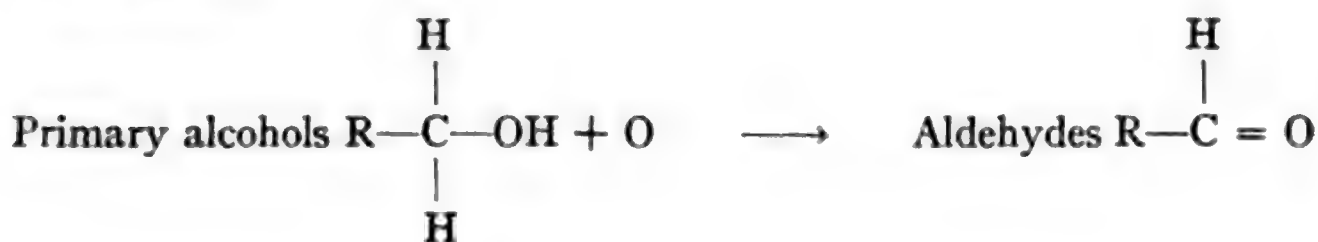
By the oxidation of one to hydroxyl and the loss of water, leaving a doubly linked oxygen, there will still be *one* unchanged hydrogen united to the carbon so that the group $\text{—CH}_2\text{OH}$ becomes —CHO , *i.e.*, the aldehyde group.

Oxidation of Secondary Alcohols.—In the *secondary* alcohol group (—CHOH—) there is only *one* hydrogen in addition to the hydroxyl group so that on its conversion into hydroxyl and the subsequent loss of water there is left *no* hydrogen united to this carbon, and we obtain

|
the ketone group, $\text{—C} = \text{O}$.

Oxidation of Tertiary Alcohols.—In the case of *tertiary* alcohols it is a fact that on oxidation they yield neither aldehydes nor ketones. This agrees with our ideas as there is *no* hydrogen linked to the carbon which has the hydroxyl. Oxidation, therefore, does not take place readily nor without breaking the carbon chain.

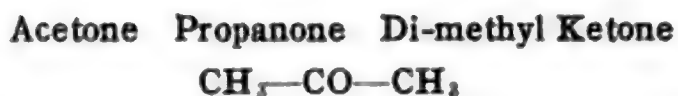
Distinguishing Reactions of the Three Classes of Alcohols.—This distinction between primary, secondary and tertiary alcohols is of fundamental importance and is the characteristic difference that is used to tell whether an alcohol belongs to one class or another. To put it all together



Comparison of Aldehydes and Ketones.—The difference between aldehydes and ketones in their structure is simply that in ketones the

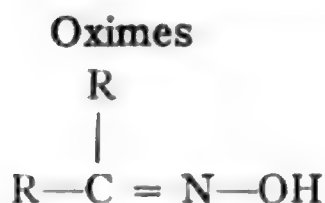
bivalent *carbonyl group* is linked to *two radicals* while in aldehydes it is linked to *one radical* and to *one hydrogen*. The characteristic reactions of aldehydes depending upon the carbonyl group we would thus expect to take place with ketones also. This is true, for ketones, like aldehydes, form addition products with hydrogen cyanide and sodium acid sulphite. With ammonia, however, they do not form simple addition products but lose water so that the resulting compounds are not of the same character as aldehyde ammonia. Likewise the reactions of the aldehydes, which depend upon the presence of the hydrogen linked to the carbonyl carbon group, we should not expect to occur with the ketones. This is true in the case of their oxidation as they yield entirely different products. It is also true in regard to transformation into polymeric forms which does not take place with ketones. This would indicate that the polymerization of aldehydes is in some way associated with the presence of hydrogen linked to the carbonyl carbon. As ketones do not oxidize readily they differ from the aldehydes in not being good reducing agents.

Names of Ketones.—The systematic names of the ketones differ from those of the alcohols and aldehydes only in the termination *one* which is added to the name of the hydrocarbon. The position of the carbonyl is denoted as in other cases by the number following.

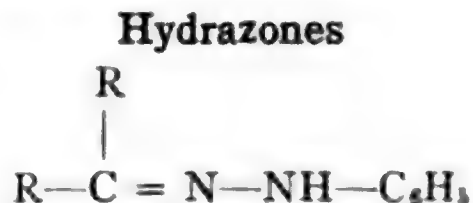


The only ketone which we shall consider is **acetone**, $\text{CH}_3\text{—CO—CH}_3$, or **propanone**, also called **di-methyl ketone**. Acetone is a liquid that boils at 56.5° . It has a peculiar odor, and is soluble in all proportions in water. It is a valuable solvent for many organic substances and is used in the manufacture of explosives and in important synthetic reactions. It is the third important constituent of crude wood alcohol or pyroligneous acid, being formed as a product of the dry distillation of wood. Table XIII gives the names, formulas and boiling points of a few of the more common and important ketones.

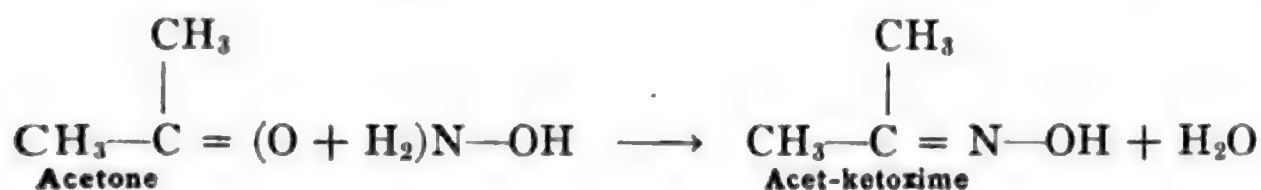
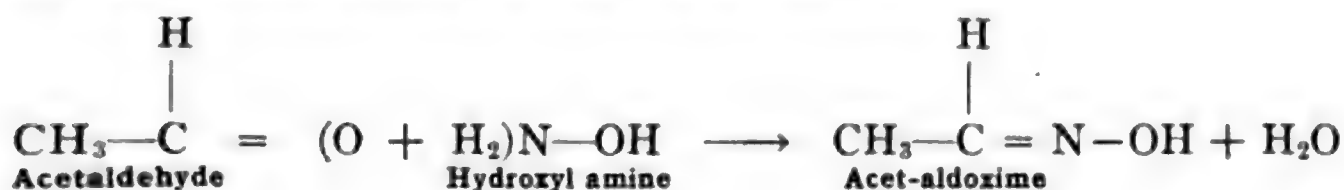
DERIVATIVES OF ALDEHYDES AND KETONES



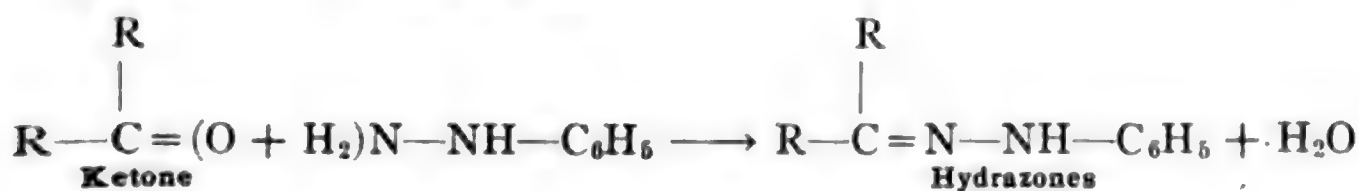
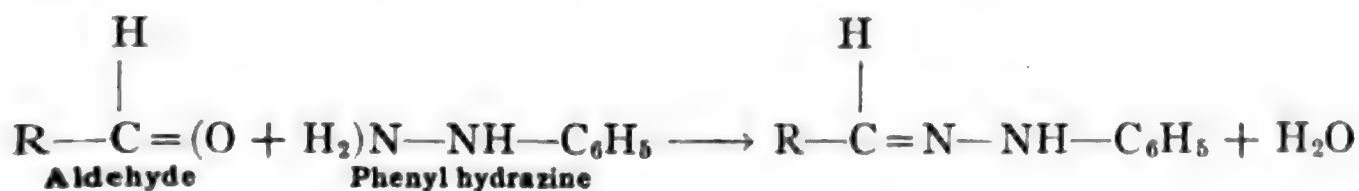
and



Two classes of compounds should be mentioned at this time as they are derivatives of both aldehydes and ketones. We have spoken of the two compounds **hydroxyl amine**, $\text{NH}_2(\text{OH})$ and **phenylhydrazine**, $\text{C}_6\text{H}_5\text{—NH—NH}_2$ (p. 63). With compounds containing the carbonyl group these react in a similar way. The *oxygen of the carbonyl unites with the two hydrogens of the primary amine group* forming water, the two residues uniting to form a new compound.



The compounds formed with hydroxylamine are known as *oximes* those from aldehydes are called *ald-oximes* and those from ketones *ket-oximes*. The compounds resulting from the action of phenylhydrazine on aldehydes or ketones are known as *hydrazones*.



These two reactions are characteristic of the carbonyl group and are used in determining its presence in compounds. They have been of especial importance in the study of the sugars.

(C) ACIDS R—COOH

Relation to Alcohols.—The third class of oxidation products of the alcohols consists of the acids. Strictly speaking they should be called oxidation products of aldehydes, but as the latter are formed directly from the alcohols the acids are generally included in the group of alcohol oxidation products.

Composition and Constitution.—We have already spoken of the fact that the aldehydes are named from the acids to which they are related. When **formaldehyde** is oxidized it yields **formic acid** which has the composition CH_2O_2 and **acetaldehyde** yields **acetic acid**, $\text{C}_2\text{H}_4\text{O}_2$. Each acid contains *one* atom of oxygen more than the aldehyde. The relation in composition between hydrocarbons, alcohols, aldehydes and acids is

Hydrocarbon	Alcohol	Aldehyde	Acid
CH_4 Methane	CH_4O Methyl alcohol Methanol	CH_2O Formaldehyde Methanal	CH_2O_2 Formic acid Methanoic acid
C_2H_6 Ethane	$\text{C}_2\text{H}_6\text{O}$ Ethyl alcohol Ethanol	$\text{C}_2\text{H}_4\text{O}$ Acetaldehyde Ethanal	$\text{C}_2\text{H}_4\text{O}_2$ Acetic acid Ethanoic acid

What is the constitution of the acids and does it explain them as oxidation products of alcohols and aldehydes?

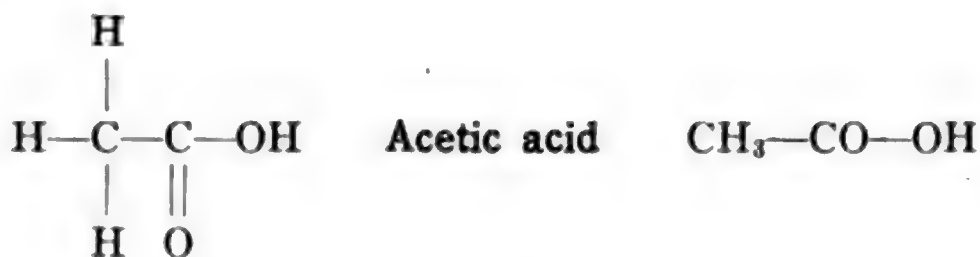
Action of Metals.—The action of metals on acids shows, in case they are mono-basic, that in them *one* hydrogen atom is different from the others as it is *replaceable by metals* with the formation of salts.

Action of PCl_5 .—The action of phosphorus pentachloride proves that acids contain a *hydroxyl group* as products are formed exactly analogous to those obtained from alcohol (p. 81). The products are hydrochloric acid, phosphorus oxychloride and a derivative of the acid which contains one chlorine atom in place of one oxygen and one hydrogen as hydroxyl.

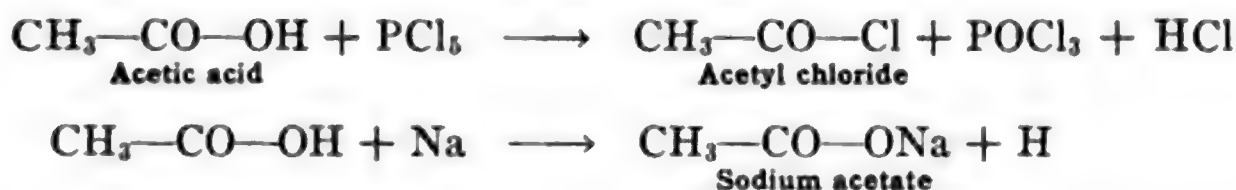
In these reactions of acetic acid with phosphorus pentachloride and with metals, only *one* oxygen and *one* hydrogen are involved showing that the other oxygen and three of the hydrogens are different. From this we can conclude at least that the formula for acetic acid, $\text{C}_2\text{H}_4\text{O}_2$, may be written $\text{C}_2\text{H}_3\text{O}(\text{OH})$. Are the three remaining hydrogen atoms linked to one carbon as methyl, ($-\text{CH}_3$)? The synthesis of acetic acid by the oxidation of ethyl alcohol which contains the methyl group would indicate that this is so. We have, however, better evidence than this.

Presence of Methyl.—Methyl cyanide, which is the cyanide substitution product of methane, CH_3-CN , yields **acetic acid** when boiled with water. The methyl group must, therefore, undoubtedly be present in acetic acid. This would further make it probable that the other

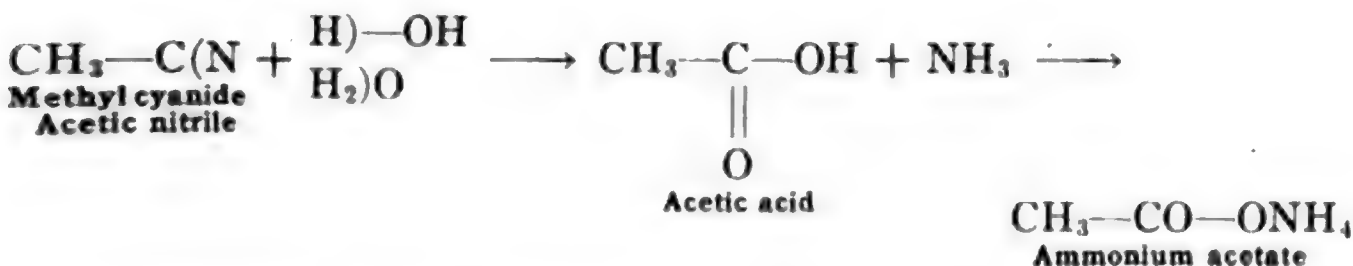
oxygen and other carbon are linked as carbonyl and the complete structural formula would be,



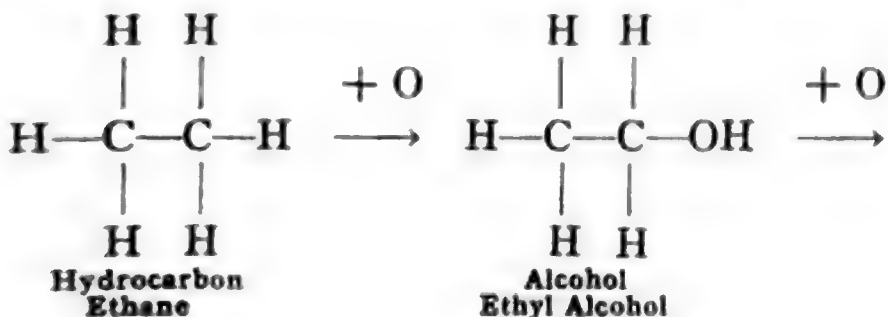
The group ($-\text{COOH}$) is known as the *carboxyl* group. The general formula for acids of this class is then $\text{R}-\text{COOH}$ or $(\text{C}_n\text{H}_{2n+1})-\text{COOH}$ which agrees with our conception of the valence of carbon. The reaction between acetic acid and phosphorus pentachloride and that between the acid and sodium may then be written as follows:

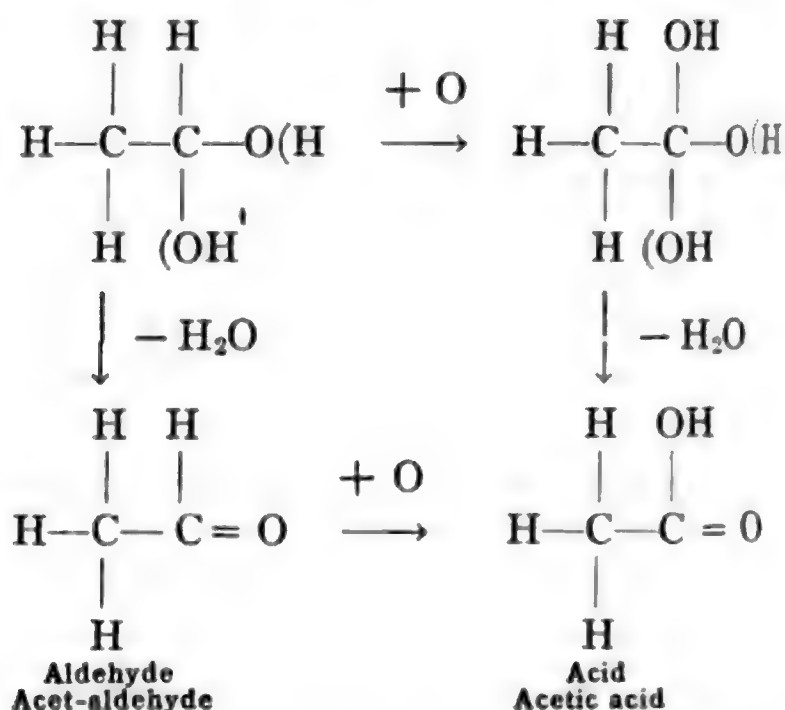


The synthesis of acetic acid from methyl cyanide or acetic nitrile by the action of water may also be written now as follows:

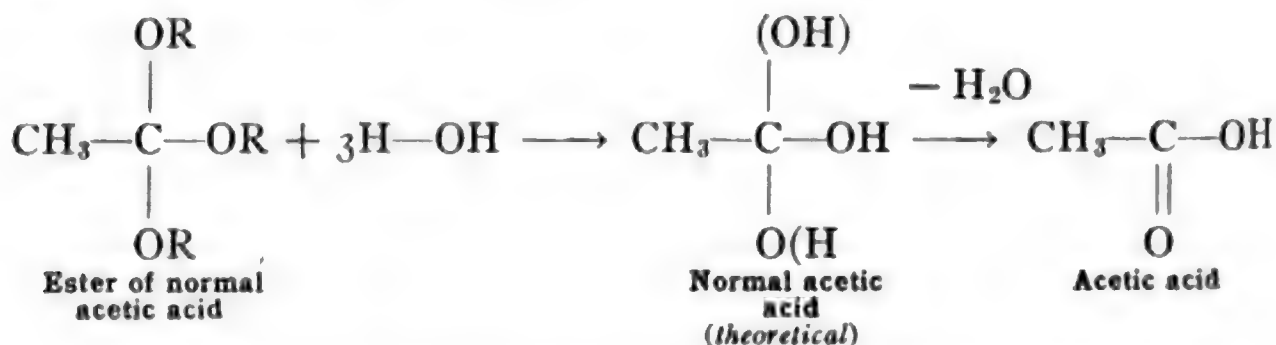


Oxidation Reactions.—This constitution of acids is in accord with the process of the oxidation of hydrogen linked to carbon, as was discussed under aldehydes and ketones. The remaining hydrogen of the aldehyde group is converted into hydroxyl and we may represent the entire oxidation from hydrocarbon to acid as follows:





The strong indication even though it may not be proof that this is the mechanism of the oxidation process, is furnished by the fact that we know esters of the normal acid containing the *three OH groups*. These esters by hydrolysis yield the acid.



It is a fact also, as previously stated, that ketones do not yield acids on oxidation without breaking down and this is readily understood as there is *no* hydrogen remaining which is linked to the carbonyl carbon and thus possible of being converted into hydroxyl, *e.g.*, in **acetone**, $\text{CH}_3\text{CO}-\text{CH}_3$.

Stability of Carbon Hydrogen Groups.—In our early discussion of the paraffin hydrocarbons we spoke of the fact that their stability is a characteristic property as illustrated by their inactivity toward ordinary reagents, (*e. g.*) in oxidation reactions. This general stability of groups composed of carbon and hydrogen is strikingly confirmed by the relation of substitution products of the hydrocarbons toward oxidizing agents. The substituted hydrocarbons are always more easily oxidized than the hydrocarbons themselves and in such oxidation it is always the

Homologous Series.—The two acids, **formic** and **acetic**, are the first two members of an homologous series corresponding to the similar series of hydrocarbons and alcohols.

Hydrocarbon	Alcohol	Acid
H—CH_3 Methane	$\text{H—CH}_2\text{OH}$ Methyl alcohol Methan-ol	H—COOH Formic acid Methanoic acid
$\text{CH}_3\text{—CH}_3$ Ethane	$\text{CH}_3\text{—CH}_2\text{OH}$ Ethyl alcohol Ethan-ol	$\text{CH}_3\text{—COOH}$ Acetic acid Ethanoic acid

In formic acid the simplest member of the series the radical of the general formula R—COOH becomes simply H. The rest of the series may be illustrated by the more important members given in the following table.

Names of Acids.—The common names of the normal acids are derived from words having some relation to their occurrence or properties, *e.g.*, **butyric**, from butter, **valeric** from *Valeriana*, etc. The official names are derived by adding the termination *oic* to the root of the name for the hydrocarbon of the same number of carbon atoms. This will be understood by examining the names given in the table and comparing with the formulas.

Isomerism.—Isomerism in the case of the acids is of the same character as that of the alkyl halides and the alcohols if we consider the acids as *mono-carboxyl substitution products of the hydrocarbons*. In the five carbon acids, the **pentanoic** or **valeric acids**, we have one compound which possesses an *asymmetric carbon atom*. It is the **2-methyl butanoic-1 acid**. According to the **van't Hoff-LeBel** theory this compound should exist in three forms, *dextro*, *levo* and *inactive*. By oxidation of the fermentation amyl alcohol which is a mixture of **2-methyl butanol-1** and **2-methyl butanol-4** there is obtained a mixture of two of the valeric acids, viz., the **2-methyl butanoic-1 acid** and the **2-methyl butanoic-4**. This same mixture is found naturally in the roots of *Valeriana officinalis*. By separating out the **2-methyl butanoic-4 acid** the **2-methyl butanoic-1 acid** is obtained. This acid is inactive, but has *never, with certainty*, been separated into its optical components, though it is claimed that a *dextro* form has been obtained.

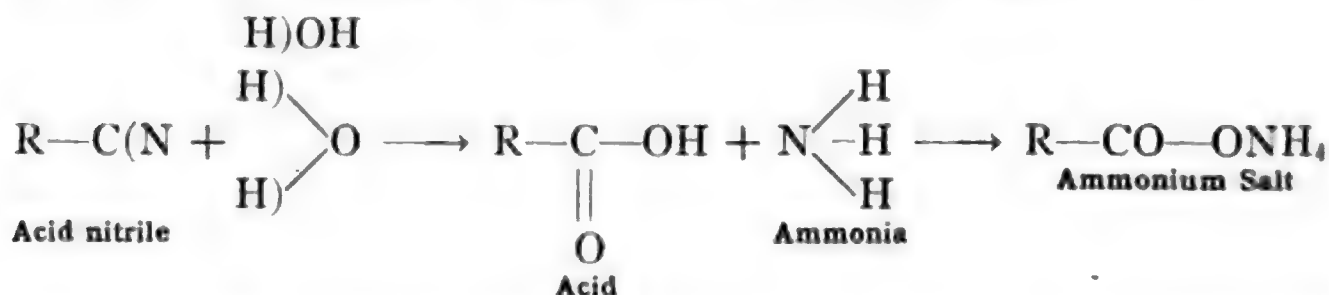
Methods of Preparation.—The general methods of preparing the acids are the following: (1) *From the acid nitriles by boiling with water*. In this reaction the carbon of the cyanogen radical of the nitrile re-

TABLE XIV.—HOMOLOGOUS SERIES OF SATURATED ACIDS. (FATTY ACIDS)

R—COOH(C_nH_{2n+1})—COOH

Common name	Official name	Formula	B.P.
Formic.....C ₁	Methanoic.....	H—COOH	101.0°
Acetic.....C ₂	Ethanoic.....	CH ₃ —COOH	120.0°
Propionic.....C ₃	Propanoic.....	CH ₃ —CH ₂ —COOH	140.9°
Butyric.....C ₄	Butanoic.....	CH ₃ —CH ₂ —CH ₂ —COOH	162.5°
Iso-butyric.....C ₄	2-Methyl propanoic.....	CH ₃ —CH—COOH CH ₃	153.5°
Valeric.....C ₅	Pentanoic.....	CH ₃ —CH ₂ —CH ₂ —CH ₂ —COOH	186.0°
Iso-valeric.....C ₅	2-Methyl butanoic-4.....	CH ₃ —CH—CH ₂ —COOH CH ₃	176.5°
Methyl ethyl acetic.....C ₅	2-Methyl butanoic-1.....	CH ₃ —CH ₂ —CH—COOH CH ₃	177.0°
Tri-methyl acetic.....C ₅	2-2-Di-methyl propanoic.....	CH ₃ —C—COOH CH ₃	163.7°
Caproic.....C ₆	Hexanoic.....	CH ₃ —CH ₂ —CH ₂ —CH ₂ —CH ₂ —COOH	205.0°
Iso-caproic.....C ₆	2-Methyl pentanoic-5.....	CH ₃ —CH—CH ₂ —CH ₂ —COOH CH ₃	201.0°
Oenanthylic.....C ₇	Heptanoic.....	CH ₃ (CH ₂) ₅ —COOH	224.0°
Caprylic.....C ₈	Octanoic.....	CH ₃ (CH ₂) ₆ —COOH	236.0°
Capric.....C ₁₀	Decanoic.....	CH ₃ (CH ₂) ₈ —COOH	270.0°
Lauric.....C ₁₂	Dodecanoic.....	CH ₃ (CH ₂) ₁₀ —COOH	M.P.
Myristic.....C ₁₄	Tetradecanoic.....	CH ₃ (CH ₂) ₁₂ —COOH	43.6°
Palmitic.....C ₁₆	Hexadecanoic.....	CH ₃ (CH ₂) ₁₄ —COOH	53.8°
Stearic.....C ₁₈	Octadecanoic.....	CH ₃ (CH ₂) ₁₆ —COOH	62.0°
Arachidic.....C ₂₀	Eicosanoic.....	CH ₃ (CH ₂) ₁₈ —COOH	69.2°
			75.0°

mains linked to the carbon of the alkyl radical. The nitrogen of the cyanogen radical, however, breaks away and with three hydrogen atoms from two molecules of water it forms ammonia. From the water there remains one oxygen and hydroxyl, (OOH), which with the cyanogen carbon forms carboxyl, (COOH). This, it will be recalled, is the proof that in the *nitrile, or cyanide, carbon is linked to carbon* (p. 68). The reaction is very clear if written as follows:



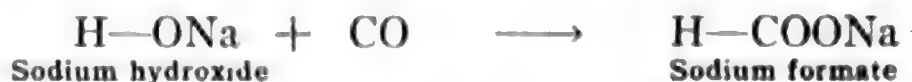
(2) *From sodium alkyls and carbon dioxide.* In this reaction the carbon dioxide seems to enter the compound directly forming the carboxyl group.



(3) *From sodium alcoholates and carbon monoxide.* This is analogous to the above, the carboxyl group being formed by the direct entrance of the carbon monoxide.



(4) In the case of formic acid this last synthesis is from **sodium hydroxide** and **carbon monoxide** and is the commercial method of making this acid.



(5) *From alcohols or aldehydes by oxidation* as previously discussed.

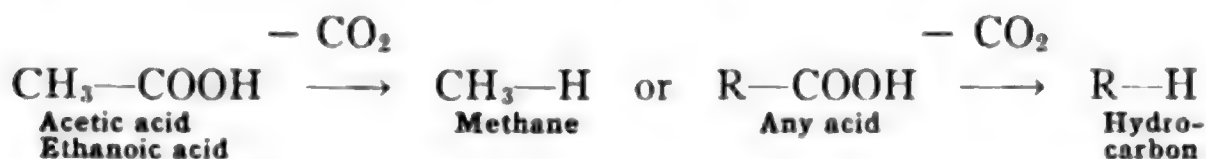


These are the general methods which do not involve other compounds than those we have already studied.

Properties.—The general relation in physical properties between the members of the homologous series of acids is like that in the homologous series of hydrocarbons and alcohols. The lower members are liquids while the higher members are wax-like solids.

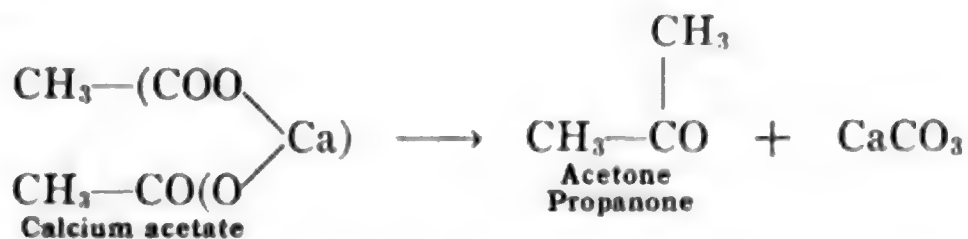
Reactions.—The acid properties of these compounds and their ability to form salts is, of course, their most prominent reaction. Several other reactions, in particular those with alcohols and phosphorus pentachloride, will be discussed under the subject of derivatives of the acids.

Hydrocarbons from Acids.—One reaction to be spoken of at this time is the transformation of the *acids into hydrocarbons*. This has already been referred to as the simplest method of preparing **methane** (p. 7). When an organic acid loses carbon dioxide it is converted into a hydrocarbon with one less carbon atom than the acid itself.

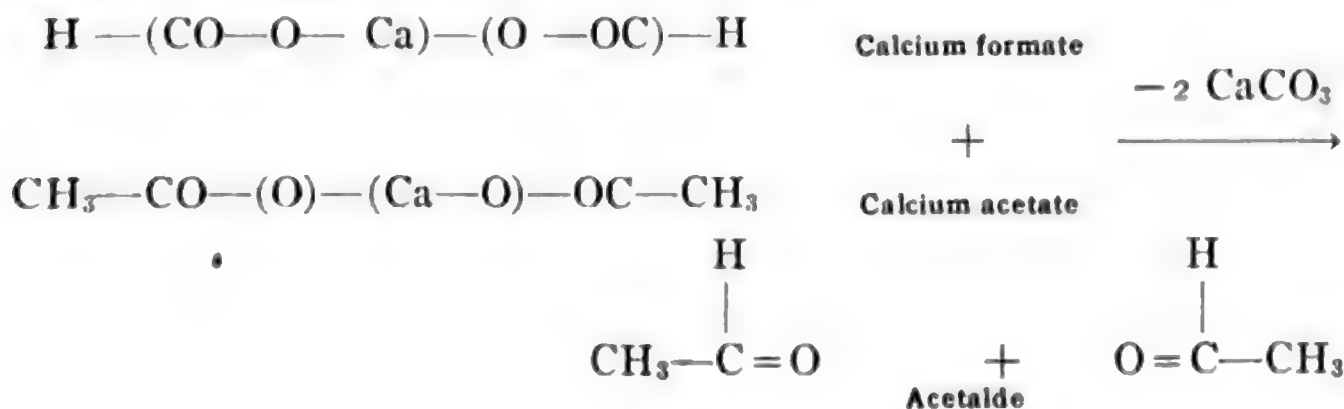


This is a general reaction for preparing hydrocarbons and is the reverse of the second general method of preparing acids as given above. It is usually accomplished by heating the acid with an alkali, *e.g.*, sodium or calcium hydroxides.

Ketones from Acids.—Another important reaction of acids is the *formation of ketones and aldehydes* by the decomposition of salts of the acids. When **calcium acetate** is heated the calcium remains combined with part of the two carboxyl groups as calcium carbonate and the two alkyl radicals become united by the remaining carbonyl group forming a *ketone*.



If a *mixture of the calcium salts of a higher acid and of formic acid* is heated an *aldehyde* results.

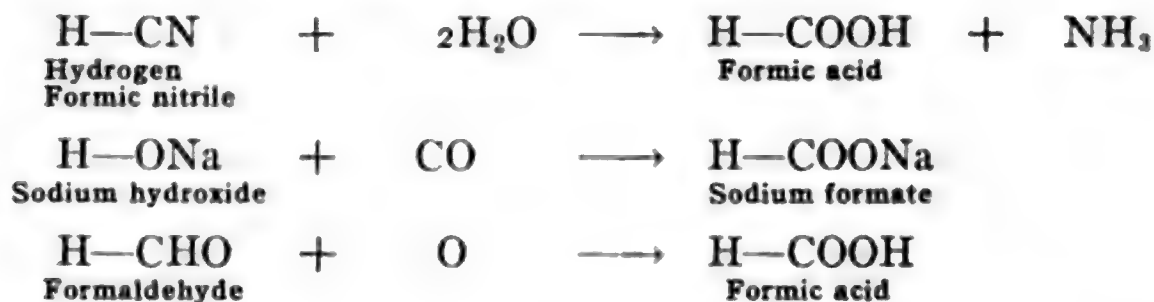


These are *general methods for the formation of ketones and aldehydes*. By the first action, if the salt of only one acid is used, the ketone will always be a simple ketone and will contain the same alkyl radicals as the acid. In case a mixture of acids other than formic acid is used the product will be partly a mixed ketone containing the two alkyl radicals of the acids used. The second reaction always yields the aldehyde corresponding to the acid other than formic.

Occurrence.—The members of this series of acids are derived from the methane series of hydrocarbons and occur very commonly in nature. In a few cases they are found free as formic acid in ants and nettles and valeric acid in the root of *Valeriana*. In most cases the acids are combined with alcohols as *esters* and as such are found in *etheral oils*, *fats* and *waxes*. This has given them the name *fatty acids*.

Formic Acid H—COOH Methanoic Acid

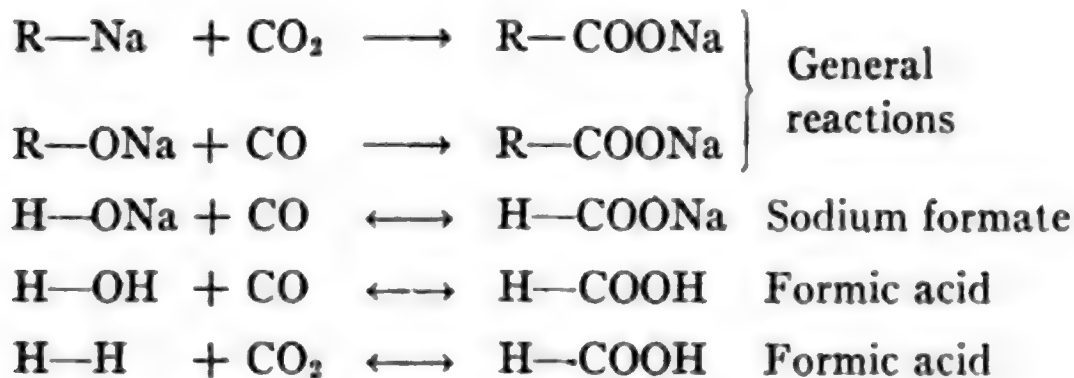
Formic acid, the simplest of the fatty acids, is found free in nature as just stated, the name for ants, viz., *Formicidæ*, giving the name to the acid. It is a liquid, B. P. 101° with a very sharp odor and an irritating or blistering effect upon the skin. It yields well crystallized salts of the metals especially of copper, lead and calcium. It may be prepared by the general methods given above, *e.g.*:



The commercial method of making formic acid is by the second reaction. It is of especial importance in the manufacture of **oxalic acid** and will therefore be discussed in detail in connection with that acid (p. 269). In the laboratory it is generally made by heating **oxalic acid** in **glycerol**. The oxalic acid breaks down and yields formic acid as will be shown under oxalic acid. When heated with sulphuric acid formic acid breaks down and yields **water** and **carbon monoxide**, which is the reverse of the second reaction just given.



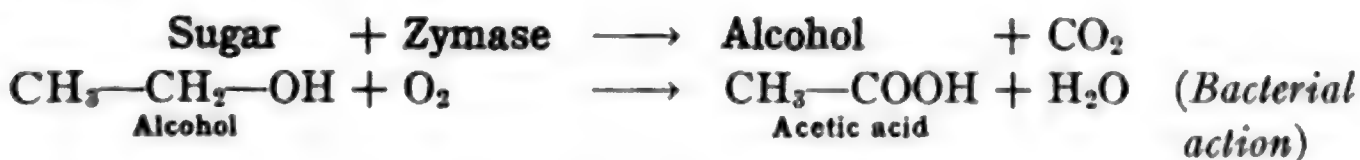
A study of the general methods of preparation as given under 2, 3, and 4 shows that formic acid is the direct reduction product of carbon dioxide, CO_2 .



The two reactions with carbon monoxide become reversible at higher temperatures so that when formic acid is heated it breaks down to $\text{CO} + \text{H}_2\text{O}$ as just explained.

Acetic Acid $\text{CH}_3\text{—COOH}$ **Ethanoic Acid**

Acetic Fermentation.—Acetic acid in addition to its occurrence in nature in the form of esters is produced on the large scale by the *acid fermentation* (oxidation) of the alcohol obtained as the result of fermenting fruit juices which contain sugar, especially apple juice or *cider*, and *wine*. When the sugar present in cider is fermented, due to the action of the enzyme zymase, alcohol is produced (p. 95). This alcohol is then oxidized through the activity of an aerobic bacterial organism *Bacterium aceti*, which is present naturally in the fruit juice. The product is acetic acid.



Vinegar.—Acetic acid produced by this natural process is known as *vinegar*. As vinegar may be made by the acetic fermentation of any natural alcoholic liquid such as cider, wine or malt liquors it will possess characteristic properties depending upon its source. Naturally this process is slow, the cider being allowed to stand for a long time with access to the air. Industrially the process is much hastened by allowing the weak alcoholic liquid to flow slowly over beech wood shavings which are covered with the *bacterium aceti* while the whole is kept well aerated and at a temperature of about 33° . These processes all produce a dilute solution of acetic acid known as vinegar which contains from

about 3.0 to 6.0 per cent (cider vinegar, U. S.) or 6.0 to 12.0 per cent (wine vinegar, France) of pure acetic acid.

Wood Distillation.—Acetic acid of greater strength than this is made by the destructive distillation of wood. This process has been described under the preparation of methyl alcohol (wood alcohol). The distillate obtained from the wood and known as *pyroligneous acid* contains about 4 to 8 per cent of pure acetic acid. This is separated from the alcohol, acetone and other substances present by conversion into the calcium or sodium salt. The acid is again set free by treatment of the calcium acetate with sulphuric acid and is then distilled. In this way acid of about 90 per cent is obtained. Dilute acetic acid so made is termed wood vinegar. In 1916 something over 100,000,000 pounds of acetic acid were produced from the 1,100,000 cords of wood distilled in the U. S. which at the same time yielded the 10 to 11 million gallons of methyl alcohol as given on page 95.

Glacial Acetic Acid.—Glacial acetic acid has the same relation to ordinary acetic acid that absolute alcohol has to ordinary alcohol, *i.e.*, it is 100 per cent. acid. It is obtained from strong acetic acid by fractional distillation. Pure acetic acid crystallizes at 16.7° , hence the name **glacial acetic acid**. It is a liquid, boiling point 120° , sp. gr. 1.05, with a sharp odor and irritating effect upon the skin similar to formic acid but not so strong. The salts of acetic acid are mostly crystalline compounds, the important ones being those of **sodium, potassium, ammonium, calcium, iron, aluminium, copper** and **lead**. The iron and aluminium acetates are used as mordants in dyeing. The copper acetate is a constituent of several insecticides (Paris green, etc.), and the lead acetates are used in medicine and in making white lead, basic lead carbonate, for paints. The chief uses of acetic acid other than as vinegar are in the preparation of **acetone** (p. 133) and the salts mentioned above. Also both acetic acid itself and acetone are used in the manufacture of smokeless powder and high explosives.

Higher Acids

The only higher fatty acids which will be mentioned are:

Butyric acid, Butanoic, C_3H_7-COOH , occurring as an ester of glycerol in butter.

Valeric acids, Pentanoic, C_4H_9-COOH , found free and as ester in *Valeriana officinalis*.

Capric acid,	Hexanoic, $C_6H_{11}-COOH$,	occurring as an ester of glycerol in goat's milk.
Palmitic acid,	$C_{15}H_{31}-COOH$	which, as esters of glycerol, are the chief constituents of many fats and oils.
Stearic acid,	$C_{17}H_{35}-COOH$	
Arachidic acid,	$C_{19}H_{39}-COOH$,	which occurs in peanut oil as an ester of glycerol.

DERIVATIVES OF ACIDS

1. SALTS $R-COON$

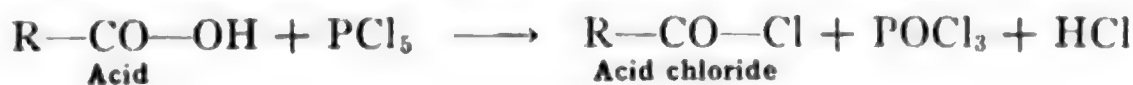
We shall consider now several different classes of compounds which are formed from the acids, *i.e.*, derivatives of the acids. The simplest derivatives are the metal salts formed by neutralizing the acid with a base.



In these compounds the hydrogen of the hydroxyl is replaced by a metal. As there is only one hydroxyl hydrogen in the acids containing only one carboxyl group they are mono-basic and yield only one class of salts, *viz.*, neutral salts. It will not be necessary at this time to consider these compounds at any length as they have been sufficiently described under the acids themselves. The most common acids, *e.g.*, formic and acetic acid, form well crystallized salts with practically all of the metals, and these salts are all soluble in water. All of these salts on treatment with stronger acids, hydrochloric or sulphuric, yield the free organic acid.

2. ACID CHLORIDES $R-CO-Cl$ Acetyl Chloride $CH_3-CO-Cl$

The reaction which proves the presence of the hydroxyl group in acids is that with phosphorus penta-chloride.



The compound formed, $R-CO-Cl$, in which *one chlorine atom has replaced the acid hydroxyl*, is known as an *acid chloride*. The acid

chlorides may also be formed by the reaction of hydrochloric acid upon the acid.



This, however, is not a complete reaction as it is quickly reversible, the water acting on the acid chloride reforming the acid. In fact this reverse reaction is the more prominent and all acid chlorides form acids when decomposed with water. With the lower acid chlorides the action is so violent that it must be cautiously brought about and even traces of moisture will react so that acid chlorides fume when exposed to the air. With some of the higher acids their chlorides react less quickly with water. The ease with which chlorine in acid chlorides is replaced by hydroxyl proves that the union of chlorine in the group $\text{R}-\text{CO}-\text{Cl}$ is different from that in alkyl halides, $\text{R}-\text{Cl}$. The acid radical, $(\text{R}-\text{CO}-)$, is known in general as the *acyl* radical.

Acyl Radical.—The names of the acid chlorides are derived from the names of the acids by changing the termination *ic* to *yl*. Thus, $\text{CH}_3-\text{CO}-\text{Cl}$ is **acetyl chloride** or **ethanoyl chloride**. The acid chlorides of the lower acids are liquids which possess a very penetrating and disagreeable odor and boil at a lower temperature than the corresponding acid. Analogous compounds of bromine and iodine are formed by the action of **phosphorus tri-bromide** or **phosphorus tri-iodide** on the acids. These are:



The only compound we shall mention is the acid chloride of acetic acid, **acetyl chloride**, $\text{CH}_3-\text{CO}-\text{Cl}$, *ethanoyl chloride*. This is a liquid, boiling point 51° . It is prepared by the first method given.

Synthetic Use.—On account of the activity of the acid chlorides they are of great importance as synthetic reagents by means of which the *acyl* radical may be united to other radicals. The most important reactions in which the acid chlorides are used are the following:

(1) *Formation of anhydrides of the acids,*



(2) *Formation of esters,*



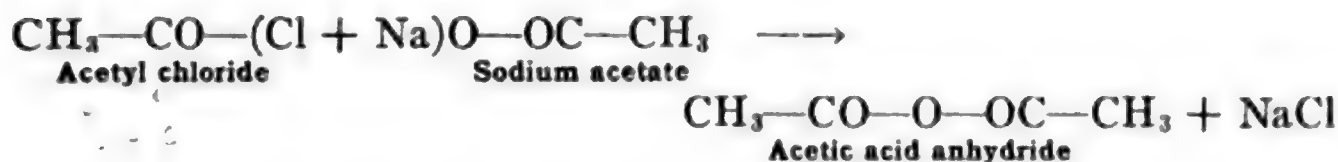
(3) *Formation of amides or ammonia derivatives,*



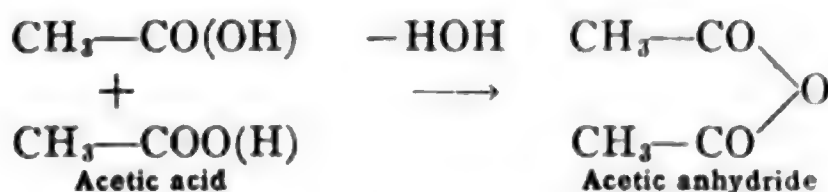
These reactions will now be considered in connection with the compounds which they form.



The acid anhydrides, as just stated, are formed when an *acid chloride acts upon an acid*, e.g., **acetyl chloride** upon **acetic acid**. The reaction takes place much better if instead of the free acid the *sodium salt* of the acid is used,

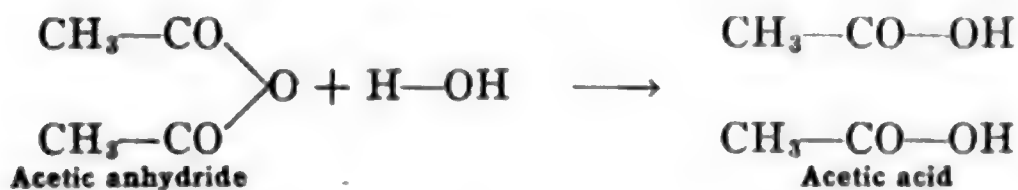


This is due to the fact that the other product of the reaction, viz., **sodium chloride**, does not act upon the anhydride and cause a reversible action as is true when hydrochloric acid is the other product. As the chlorine of the acid chloride which has replaced the *hydroxyl* of the acid removes the hydroxyl *hydrogen* from a new acid molecule it shows that the compound formed is an *anhydride of two molecules of acid*,



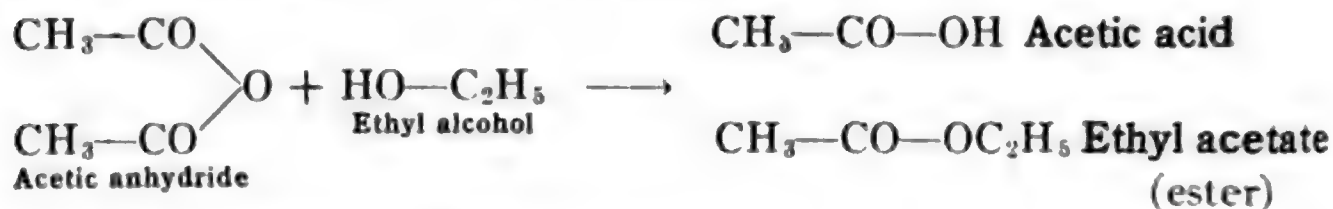
This is proven also by the fact that some anhydrides may be formed by treating the acid itself with dehydrating agents.

Reaction with Water.—As would be expected the *acid anhydrides react readily with water and reform the acid*.

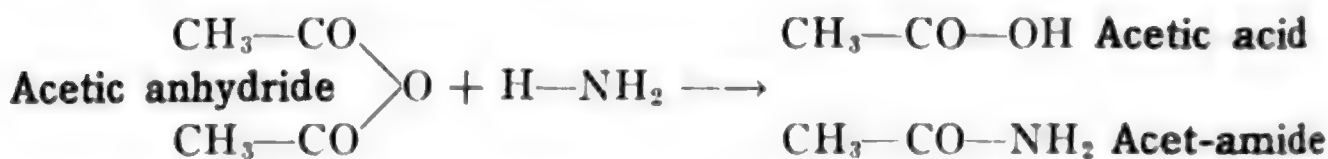


With Alcohol.—As alcohols are water type compounds we find that the anhydrides react with them in the same way as with water,

one of the products being the *free acid* and the other the *ester*. This gives another general method of preparing the esters.



With Ammonia.—With ammonia the acid anhydrides form *amides* just as do the acid chlorides,



The last two reactions will be taken up again in the following sections.

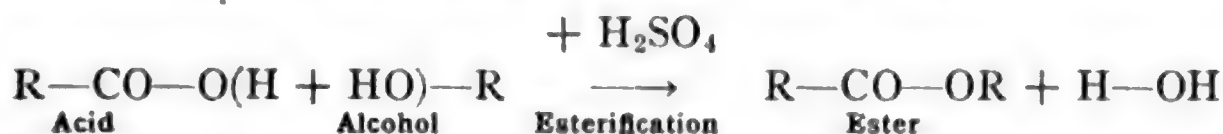
It will be noted that in all of the reactions of the anhydrides the tendency is to reform the acid by removing *one hydrogen* from the other compound present. The remaining *acyl* group then unites with the residue of the reagent and a new compound is formed. The character of the new compound depends upon the residue of the reagent. With water H—OH we obtain the *hydroxyl* compound of the acyl radical, that is, the *acid* itself, while with alcohols we obtain the *alkyl-oxyl* compound of the radical, *i.e.*, an *ester*, and with ammonia the *amino*, (—NH_2), compound of the acyl radical, *i.e.*, an *amide*.

4. ESTERS R—CO—OR ETHEREAL SALTS

The nature of *esters* or *ethereal salts* has been fully discussed already in connection with the esters of inorganic acids and alcohols (p. 102). The name salts applies because they are formed by neutralizing an alcohol, acting as a base, with an acid. It must be emphasized, however, that in so terming these compounds salts we do not mean this to apply in a physical chemical sense as describing their properties in solution in accordance with the electrolytic theory of ionic dissociation. We are dealing here with questions of composition and constitution. Ethereal salts differ from metal salts, at least as to the degree of their dissociation into ions when in solution.

Esterification.—As the organic acids which we are considering contain only *one carboxyl* group they are mono-basic, *i.e.*, they contain only *one acid hydrogen*, the *hydroxyl hydrogen*, which is replaceable by metals. They therefore react molecule for molecule with the

mono-hydroxy alcohols in the formation of esters. The reaction is termed *esterification* and is accomplished by treating the acid with the alcohol in presence of some *dehydrating agent*, e.g., **sulphuric acid**.

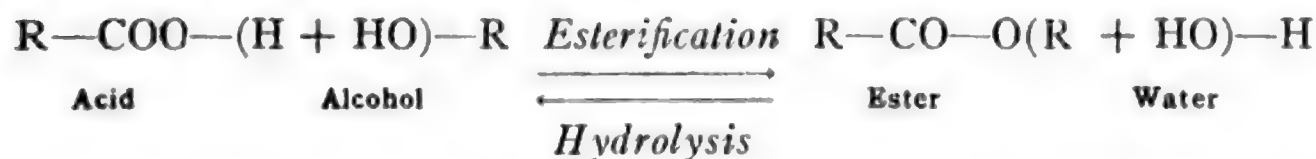


The general formula for esters of the organic acids is, therefore, R—CO—OR or Acyl-O-Alkyl.

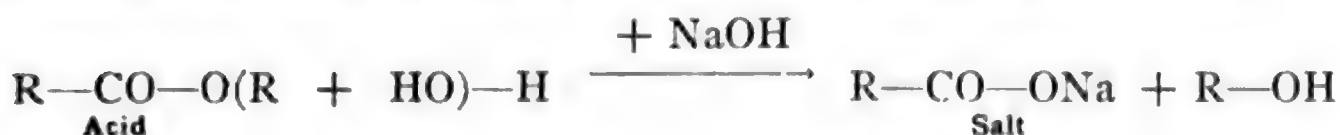
Hydrolysis.—These esters of the organic acids react as those of the inorganic acids. The most important reaction is their *decomposition with water* by which the *alcohol* and the *acid* are reformed. As the reaction involves simply the taking up of the elements of water it is termed an action of *hydrolysis*.



This reaction and the preceding one are the reverse of each other and the two may be written as *one reversible reaction* as follows:



In the presence of an alkali hydrolysis of an ester yields not the free acid but the *salt* of the acid and the reaction is then non-reversible.



Saponification.—As we shall see later, this is the kind of reaction which takes place when *soap* is made from fats and on that account it is termed an action of *saponification*. In this way the acids are obtained as salts from the naturally occurring fats, oils and waxes in which they are present in the form of esters. *The hydrolysis of esters or ethereal salts is then the general reaction by which, with the taking up of the elements of water, an ester is reconverted into the two compounds from which it was formed, viz., into an acid and an alcohol.* *Esterification and hydrolysis or saponification* are, therefore, complementary names applying to the *reversible reaction effecting the synthesis and decomposition of esters*. The reversible character of the reactions of esterification and

hydrolysis is shown by the fact that, under different physical conditions such as temperature and concentration, the amount of ester formed and also the rate at which it is formed, *i.e.*, the speed of the reaction, varies. This makes the reaction a most valuable one to study from a physical chemical standpoint. The investigation of such problems as the *law of mass action*, *chemical equilibrium*, the *relation of constitution* to the *speed of reaction*, *rate of esterification* or degree or *rule of saponification*, is greatly aided by the study of the esters. These problems and the facts that have been made known by this study are not, however, such as we wish to consider at this time in a general presentation of organic chemistry.

Names of Esters.—Considering these compounds as ethereal salts they are named on the same principal as metal salts, the name of the alkyl radical being used in place of that of the metal. The ester of **ethyl alcohol** and **acetic acid**, $\text{CH}_3\text{COOC}_2\text{H}_5$, being called **ethyl acetate** or **ethyl ethanoate**. Considering them as esters they are named as follows: **ethyl acetate** is **acetic acid ethyl ester** or **ethanoic acid ethane ester**.

Isomerism.—Isomerism in the esters may be due to several causes analogous to those given in the case of the ethers and the ketones.

(1) *Isomerism due to the isomeric nature of the acyl or alkyl radicals present, e.g.:*



Propyl butyrate
Butanoic acid propane-1-ester



Iso-propyl butyrate
Butanoic acid propane-2-ester

(2) *Isomerism due to different acyl or alkyl radicals which make the total carbon content the same, e.g.:*

Ethyl propionate	$\text{CH}_3-\text{CH}_2-\text{CO}-\text{OCH}_2-\text{CH}_3$	Propanoic acid ethane ester
Methyl butyrate	$\text{CH}_3-\text{CH}_2-\text{CH}_2-\text{CO}-\text{OCH}_3$	Butanoic acid methane ester
Propyl acetate	$\text{CH}_3-\text{CO}-\text{OCH}_2-\text{CH}_2-\text{CH}_3$	Ethanoic acid propane ester

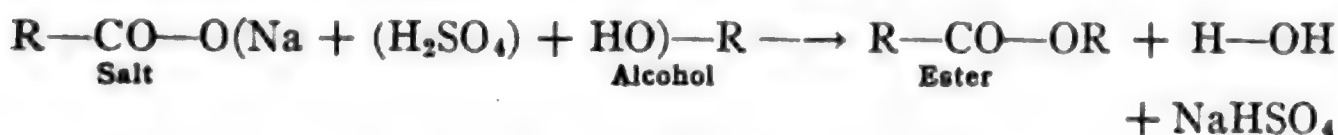
(3) *Isomerism of the esters with a different group of compounds of like composition*, the esters being isomeric with the acids of equal carbon content, the general formula for each being $C_nH_{2n}O_2$, *e.g.*:

Ethyl acetate $CH_3-CO-OCH_2-CH_3$ **Ethanoic acid ethane ester**

Butyric acid $CH_3-CH_2-CH_2-COOH$ **Butanoic acid**

Preparation.—There are several very important reactions by which the esters may be formed.

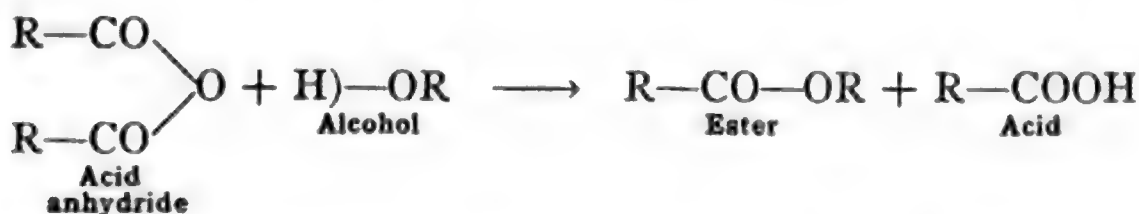
(1) *Direct esterification of alcohols and acids*, which is applicable in a good many cases. The presence of some dehydrating agent is necessary and sulphuric acid is the one usually employed. As sulphuric acid converts salts of the acids into the acids it is possible to use a salt and sulphuric acid instead of the free acid.



(2) *From an acid chloride and alcohol* as given under the acid chlorides.



(3) *From the anhydrides*, as stated in their discussion. As these always react with water type compounds, alcohols will, of course, yield the ester.



(4) *From alkyl halides and the silver salt of the acid*. The silver halide is formed and the alkyl radical takes the place of the silver thus forming the ester. This reaction shows clearly that the *alkyl radical takes the place of the metal* in the salt of the acid, *i.e.*, the ester is an *alkyl salt*.



Properties and Occurrence.—The esters of the lower acids and lower alcohols are pleasant smelling volatile liquids. This property is the origin of the word *ethereal* in the name applied to them. They

are not miscible with water though the lower members are slightly soluble in it. The higher esters are crystalline solids insoluble in water but soluble in alcohol and ether. While it is probably true that the odor of common fruits is due to the presence of esters it is not fully established as they are usually present in such small quantities.

Fruit Flavors.—The synthetically prepared esters of some of the middle members of the acid and alcohol series do, however, possess odors of certain fruits and on that account are prepared and used as *artificial fruit essences* in perfumery manufacture and as flavors. Some of these artificial essences are as follows:

Iso-amyl iso-valerate,	Iso-valeric acid iso-amyl ester,	Apple essence
Ethyl butyrate,	Butyric acid ethyl ester,	Pineapple essence
Amyl butyrate,	Butyric acid amyl ester,	Apricot essence
Iso-amyl acetate,	Acetic acid iso-amyl ester,	Pear essence

Waxes and Fats.—The *waxes* are esters of the *higher alcohols* and the *higher acids* of the paraffin series. The *fats* are esters of the *higher acids* and a *tri-basic alcohol*, **glycerol**. These will be taken up later.

5. ACID AMIDES $R-CO-NH_2$

It will be recalled that the primary amines are substitution products of the hydrocarbons in which an ($-NH_2$) group, called the *amino group*, has been substituted indirectly for a hydrogen of the hydrocarbon. They are prepared by treating an *alkyl halide with ammonia*.



Preparation from Acid Chlorides.—If instead of an alkyl halide we use an *acyl halide*, *i.e.*, an *acid chloride*, a similar reaction takes place with the formation of a compound in which the *amino group* has replaced the chlorine.

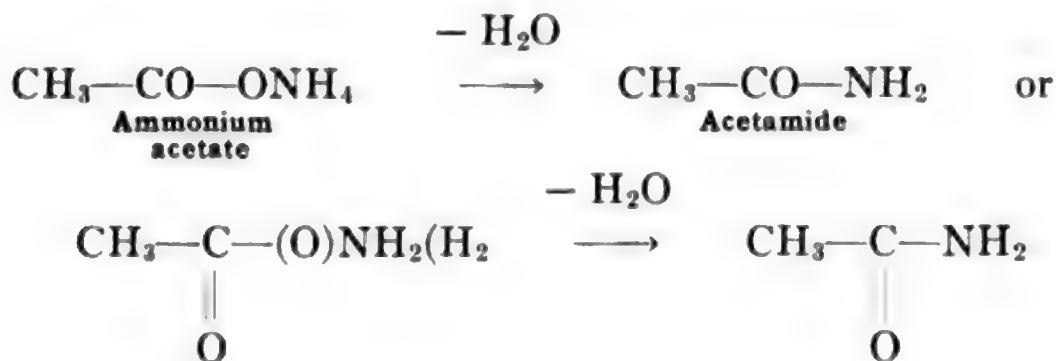


The compound so formed is clearly one in which the *amino group* is linked to the *acyl group*, the general formula being $R-CO-NH_2$. In the original acid the *hydroxyl group* has been replaced by the *amino group*. These compounds are known as *acid amides* or simply *amides*. The amide derived from acetic acid is called **acet-amide**, $CH_3-CO-NH_2$.

From Esters.—A second method of preparation similar to the first is to treat an *ester with ammonia*. In this reaction the alkyl-oxy radical of the ester reforms alcohol by means of one hydrogen from the ammonia and the acyl radical unites with the residue of the ammonia yielding the amide.



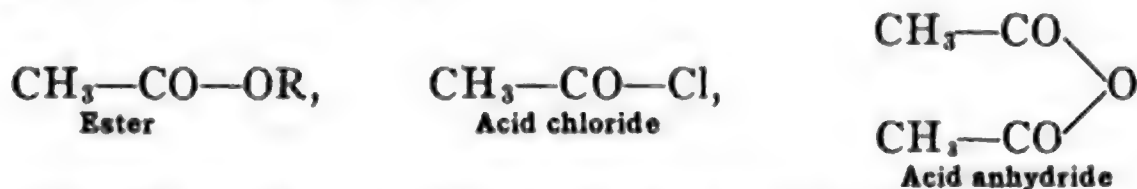
From Ammonium Salts.—Still another method for the preparation of acid amides is to simply heat the *ammonium salt of the acid*. The action taking place has been shown to result in the loss of one molecule of water.



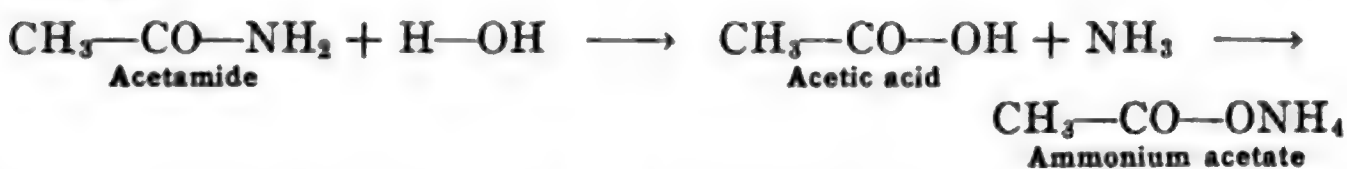
Character.—The amino substitution products of the hydrocarbons, it will be recalled, are strongly *basic* compounds, alkaline toward litmus, with ammoniacal odor and forming salts with acids analogous to ammonium salts. The acid amides, however, are found to be practically *neutral* compounds. We explain this by saying that the basic and acid portions of the compound neutralize each other, the acyl radical ($\text{CH}_3\text{CO—}$) counteracting the ammonia residue (—NH_2). That is, when the amino group is substituted in a hydrocarbon so that the nitrogen is linked to a carbon which has only hydrogen or carbon linked to it, it endows the resulting compound with a strong basic character. When, however, the amino group is substituted in the carboxyl group so that the nitrogen is linked to a carbon united to oxygen, as carbonyl, (—CO—), the basic character of the amino group is largely, if not wholly, neutralized by the acid character of the acyl group. The compound formed is *neither basic nor acid*.

Reaction with Acids.—This neutral character of the amides is, however, similar to that of the alcohols, for, like alcohols, they *act as bases toward strong acids and as acids toward strong bases*. With

or, in the presence of dehydrating agents, *they are able to lose a molecule of water*. It will be observed that of the compounds studied those which we have shown take up water, *i.e.*, are *hydrolyzed*, are compounds containing the *acyl* radical, *e.g.*:

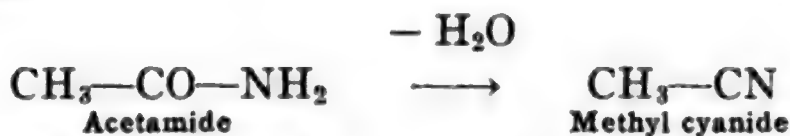


Hydrolysis of Acid Amides.—The amides are exactly analogous acyl compounds, $\text{CH}_3\text{—CO—NH}_2$, and they are quite easily hydrolyzed as follows:

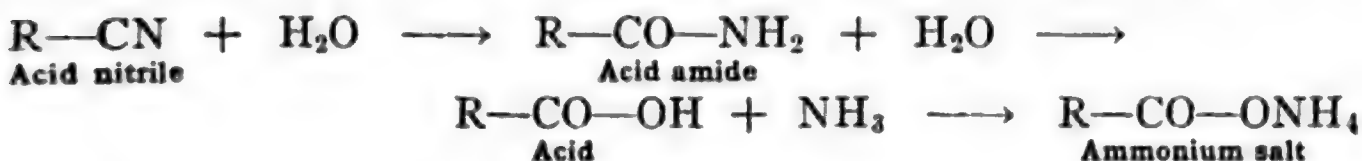


The products are the *acid* and *ammonia* which react forming the *ammonium salt* of the acid. This is, of course, simply the reverse of the third method given for preparing the amides (p. 145).

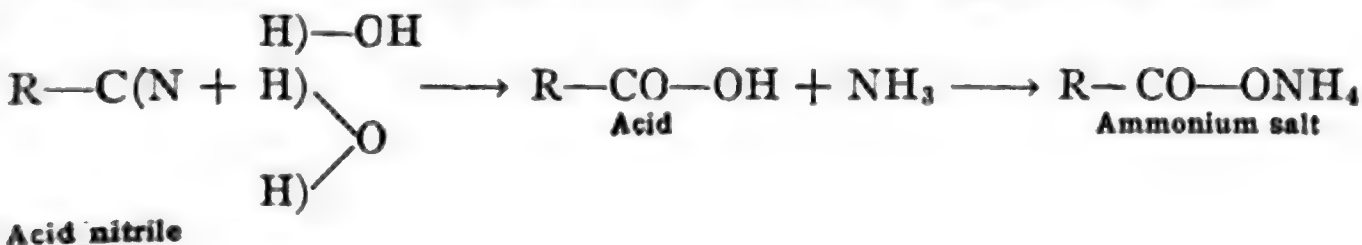
Dehydration.—When acetamide is heated with **phosphorus pentoxide**, a strong dehydrating agent, *water is lost* and the product is **methyl cyanide**.



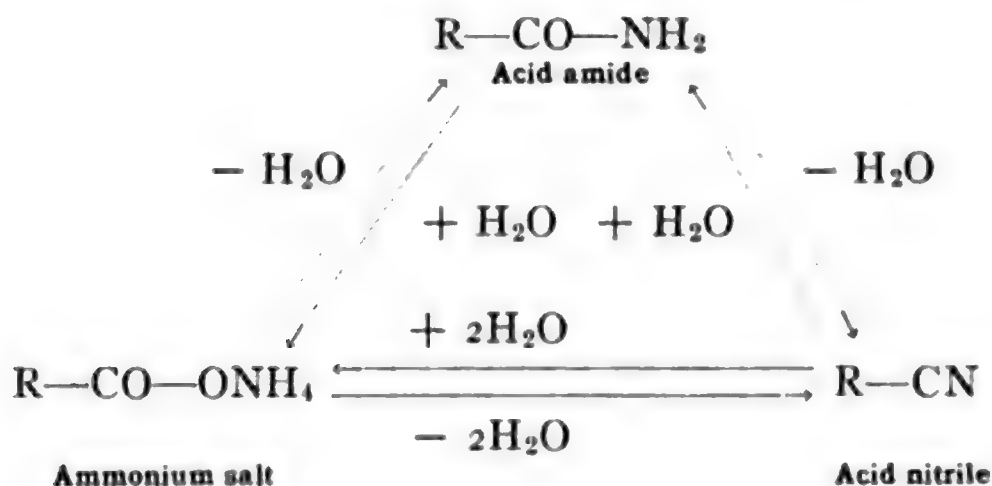
This reaction indicates that the *nitrogen in acetamide is linked to the carbon* which is in accord with both of the tautomeric formulas just given. This methyl cyanide, it will be recalled, is readily hydrolyzed to the acid requiring, however, *two* molecules of water. *Acetamide, therefore, is an intermediate step in the hydrolysis of an alkyl cyanide, acid nitrile, to an acid*. Writing the general reaction in steps we have,



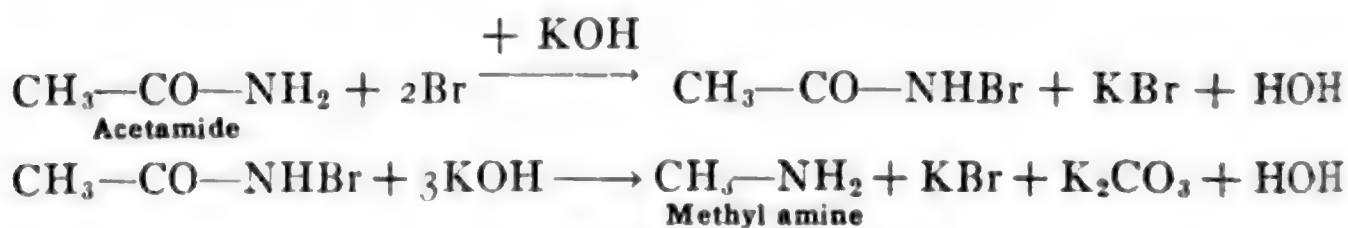
This double reaction was previously written as single in this way



The inter-relation between the acid amides, the acid nitriles and the ammonium salts of the acids may be represented as follows:



Hofmann's Reaction.—One more important reaction of the acid amides is that known as **Hofmann's reaction**. When an acid amide is treated with bromine in an alkaline solution the final product is an *alkyl amine* containing one less carbon than the amide. The steps in the reaction are represented in the case of acetamide as



Acetamide $\text{CH}_3\text{—CO—NH}_2$

The acid amides do not have many important representatives in this series of acids. The most important one is acetamide which we have used as our illustration and which may be formed by any of the methods given. The best methods of preparing acetamide are by distilling a mixture of **ethyl acetate** and concentrated **ammonium hydroxide** or by heating **ammonium acetate** in **glacial acetic acid**. The latter is usually accomplished by heating a mixture of ammonium carbonate and glacial acetic acid. The reactions involved in these preparations are those given above in general methods (2) and (3) (p. 145). Acetamide is a crystalline solid which takes up water in the air (hygroscopic). It melts at 82° . When pure it is odorless, but it usually has a characteristic odor of a dead mouse.

Recapitulation

If, before proceeding further, we glance for a moment over the ground which we have covered we see that we have considered

1. The **hydrocarbons** of the methane or **saturated series**.
2. The **simpler mono substitution products** of these hydrocarbons:
 - (a) *Halogen substitution products*.
 - (b) *Amino substitution products*.
 - (c) *Cyanogen substitution products*.
 - (d) *Hydroxyl substitution products or alcohols*.
3. **Derivatives of alcohols** :
 - (a) *Ethers* (anhydrides).
 - (b) *Esters* (ethereal salts).
4. **Oxidation products of alcohols** :
 - (a) *Aldehydes*.
 - (b) *Ketones*.
 - (c) *Acids*.
5. **Derivatives of acids** :
 - (a) *Salts*.
 - (b) *Acid chlorides*.
 - (c) *Acid anhydrides*.
 - (d) *Esters*.
 - (e) *Acid amides*.

In our discussion we have shown the relation of the different groups to each other and the reactions by which, in some cases, we may pass from one to the other. Of the hydrocarbons which are the mother substances we have considered only the one series, viz., the *saturated hydrocarbons or paraffins*. Of the substitution products or their derivatives we have studied only the simplest members, viz., the *mono-substitution products*, i.e., those resulting from the substitution in the hydrocarbon chain of *only one* element or group. As the substituting elements and groups which we have considered include all of the more common ones we may say that we have studied the principal type compounds of the saturated series.

The further treatment of the subject will therefore be simply an expansion of the general ideas which we have been considering. Such an expansion may proceed in either of two directions: *First*, a consideration of *other hydrocarbons* than those of the methane or saturated series and of derivatives obtained from them analogous to those we have

derived from methane and its homologues. *Second*, a consideration of more complex substitution products resulting from the introduction of more than one like or unlike element or group into the hydrocarbon chain, *i.e.*, *poly- or mixed-substitution products*.

It seems better to take up the first line of development and to study next those hydrocarbons which differ from the members of the saturated series but which are capable of forming the same typical substitution products and derivatives. We shall then be in a position to consider, irrespective of the character of the hydrocarbon root, the various complicated mixed compounds or poly-substitution products which are known and which are of importance.

B. SIMPLER UNSATURATED COMPOUNDS

IV. UNSATURATED HYDROCARBONS

GENERAL

In our discussion of the methane series of hydrocarbons the idea of the saturation of the molecule, or rather, the saturation of the carbon atoms in the molecule, was considered as one of the essential and distinguishing characters of the compounds. Methane, ethane and all of the hydrocarbons of this series are alike in being saturated, and this saturation is shown by the fact that none of them are able to take up, *by addition to the molecule*, any element or group of elements. Only by the reciprocal process of substitution are derivatives formed from these hydrocarbons. The general formula for the hydrocarbons of this series was shown to be C_nH_{2n+2} and all of the derivatives, thus far discussed, have resulted from the simple exchange of one or more hydrogen atoms for an equivalent amount of another element or elements, either separately or as groups.

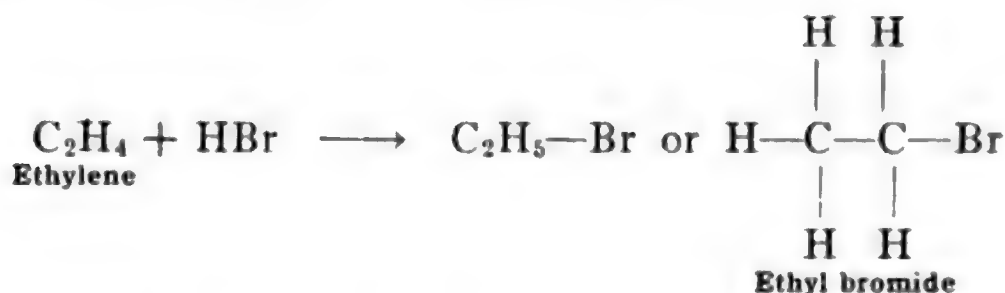
Hydrocarbons are known, however, which not only have a different general formula from that of the saturated hydrocarbons, but which show, by their properties, that they are as distinctly unsaturated as the methane hydrocarbons are saturated.

Ethylene or Ethene.—The hydrocarbon **ethylene** or *ethene* has the composition C_2H_4 . This is the first of a new homologous series of hydrocarbons of the general formula C_nH_{2n} , the members of which are related to each other in the same way as are the members of the methane series.

Addition.—When **ethylene**, C_2H_4 , is treated with **hydrobromic acid**, or with **bromine**, it does not act slowly as does methane or ethane, but most readily, and the resulting compounds are found to have the composition represented by the formulas C_2H_5Br , and $C_2H_4Br_2$. That is, *one hydrogen atom and one bromine atom or two bromine atoms are added directly to the hydrocarbon molecule.*

Unsaturation.—As the inability to take up by addition any other element or group of elements shows the saturation of the carbon atoms in methane or ethane, so, in like manner, the easy addition of hydrogen

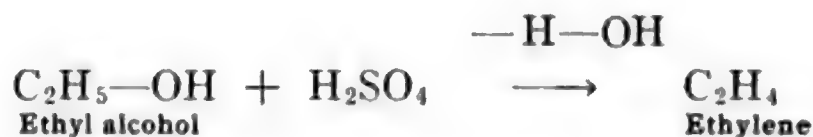
and bromine to ethylene shows, that, in it the carbon atoms must be *unsaturated*. When hydrogen bromide is added to ethylene the product is **ethyl bromide**, C_2H_5Br **monobrom ethane**.



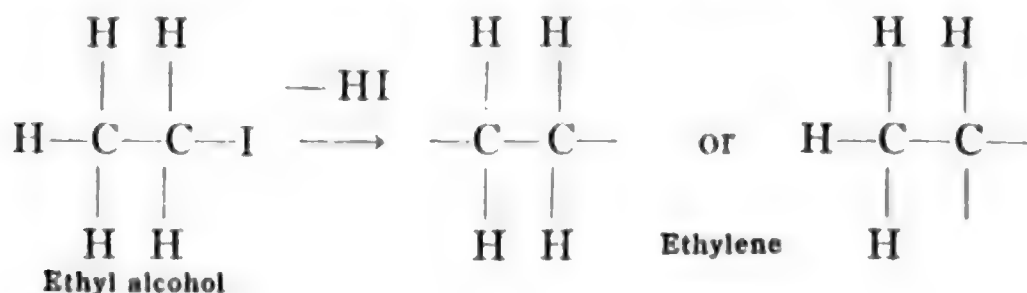
The reverse of this reaction also takes place for, when an alkyl halide, especially the iodide, is heated with alcoholic potassium hydroxide, or is passed over heated potassium hydroxide, hydrogen iodide is lost, and ethylene is obtained, as follows:



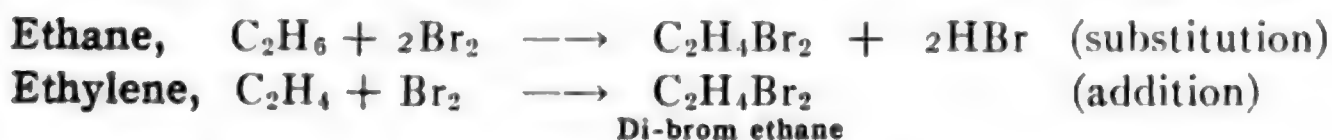
An analogous reaction to the above is the one commonly used for the preparation of ethylene. It consists in the *removal of the elements of water from ethyl alcohol* by heating with sulphuric acid or with zinc chloride:



Constitution of Ethylene.—None of these reactions, however, show anything in regard to the constitution of ethylene, for we do not know, in the case of the formation of ethylene from ethyl iodide or from ethyl alcohol, whether the hydrogen atom is removed from the same carbon group as the iodine or the hydroxyl, or from the other carbon group. The reaction may be considered as possible in either of the following ways, *i.e.*, the hydrogen and iodine may both be removed from the *same* carbon group or from *different* carbon groups.

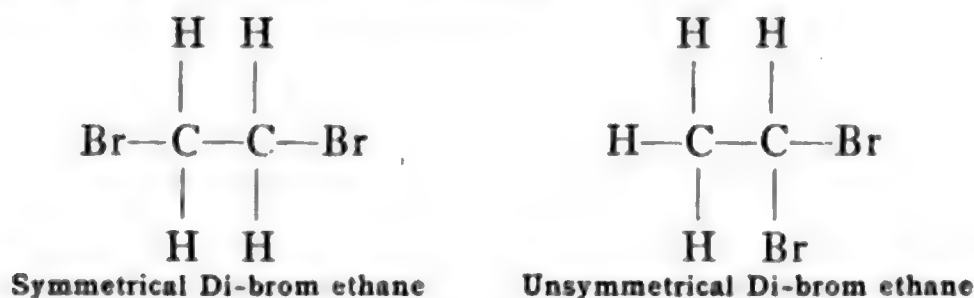


Either of the above formulas would be possible as expressing the constitution of a compound of the composition C_2H_4 . The proof as to which of these is the true one is obtained from a study of the product formed from ethylene by the addition of two bromine atoms. When bromine acts upon ethylene the product, ethylene bromide, $C_2H_4Br_2$, is found to be the same compound as one of the two isomeric di-brom ethanes which result from the substitution of two bromine atoms for two hydrogen atoms in ethane. We have, then, the two reactions:



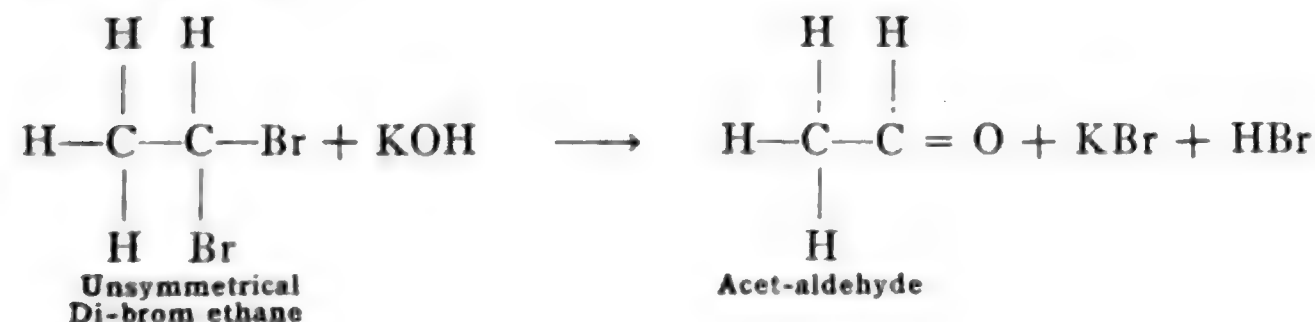
In one case the reaction is one of *substitution*, in the other it is one of *addition*.

As previously discussed (p. 53), the two di-brom ethanes are represented by the following formulas:

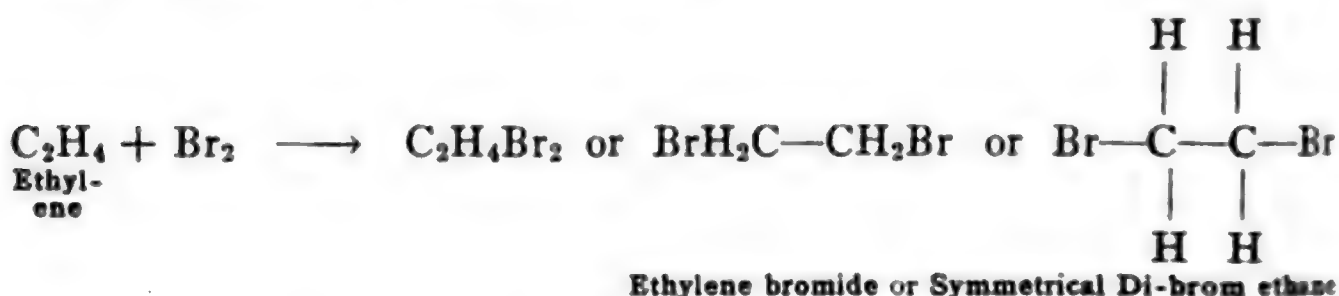


In one of these compounds the two bromine atoms replace two hydrogen atoms in the *same* carbon group giving an *unsymmetrical* di-brom ethane, while in the other they replace one hydrogen atom *in each* of two carbon groups yielding a *symmetrical* di-brom ethane.

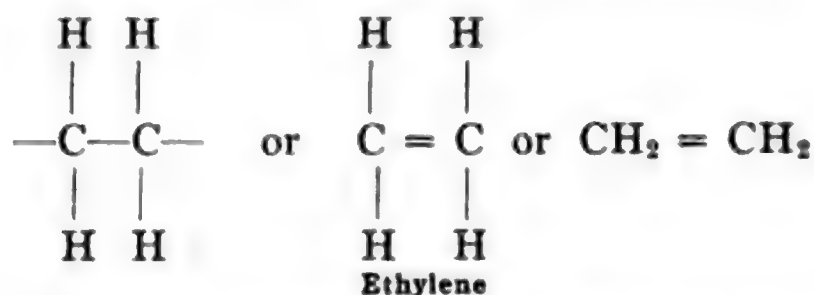
The difference between the two known compounds represented by the two formulas given above is clearly proven by their reactions. One of them when treated with potassium hydroxide yields a compound in which the two bromine atoms are replaced by one oxygen atom and the compound obtained is **acet-aldehyde**, which we know has the structure CH_3-CHO



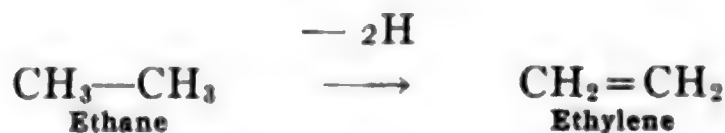
Therefore the di-brom ethane which yields acet-aldehyde must be the one in which the two bromine atoms are linked to the same carbon atom, *i.e.*, the *unsymmetrical* compound. The other compound then must have the two bromine atoms each linked to a different carbon atom, *i.e.*, it must be the *symmetrical* compound. Now it is this last compound, not the first, which is obtained when ethylene reacts with bromine and adds on two bromine atoms. For this reason it is known as **ethylene bromide**. Our reaction between ethylene and bromine must be represented, then, as follows:



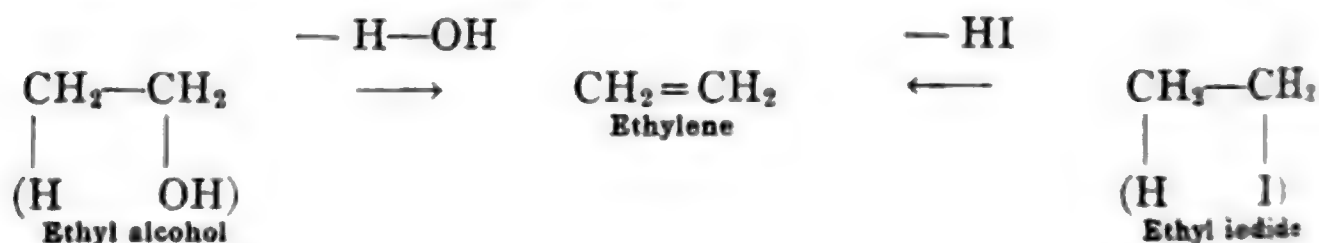
Ethylene itself, then, must be represented by the formula:



That is, it may be considered as ethane from which two hydrogen atoms have been removed, one from each carbon group:

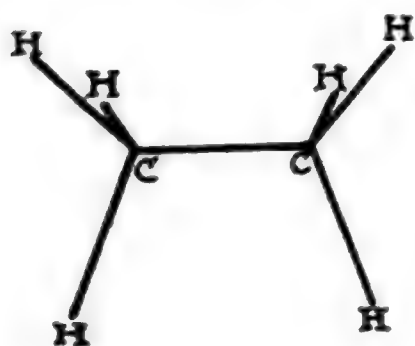


This reaction does not ordinarily take place, but the analogous reactions, *viz.*, the loss of the elements of water from ethyl alcohol, and the loss of hydrogen and iodine from ethyl iodide, do occur under the conditions previously stated. The formation of ethylene by these reactions may be represented as follows:

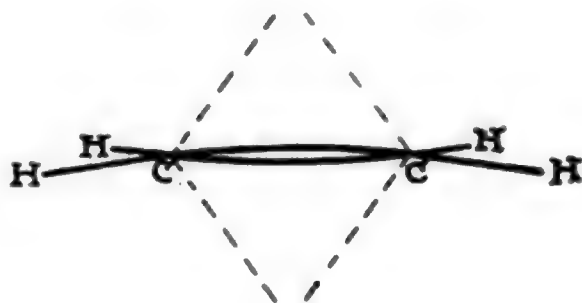


The formation of addition products with ethylene, indicating the unsaturated character of the molecule, would naturally lead to the idea that the structural formula of the compound, in accordance with its relation to ethane and in accordance with our assumption that carbon in organic compounds is tetravalent, should be that of ethane with one valence bond of each carbon atom free and unsatisfied, $\text{—CH}_2\text{—CH}_2\text{—}$.

Double Bonds.—However, the idea of free unsatisfied bonds existing in a compound does not seem to be natural and it is therefore, considered as probable that these free bonds tend to satisfy each other. Such a molecule would contain two carbon groups with the two carbon atoms doubly, not singly united. A double union, however, would seem to indicate strength, whereas, the fact is, that ethylene, in its ready formation of addition products and its general reactivity, shows itself to be *not more but less stable than ethane*. In connection with the tetrahedral theory of the space relations of carbon in organic compounds, and, as will be shown more fully when we consider the cyclic compounds in Part II, such a double union of two carbon atoms (or a ring union of more than two carbon atoms), is in fact a *less stable* condition than two carbon atoms singly united. If two carbon atoms, situated at the center of regular tetrahedra, become doubly united by two bonds of affinity indicated by the lines to the vertices of the tetrahedra, there must, of necessity, be a considerable strain produced in bringing the double union about. Such a strain would tend to produce weakness rather than strength. This may be indicated by the following figures and will be made perfectly plain by an examination of atomic models.



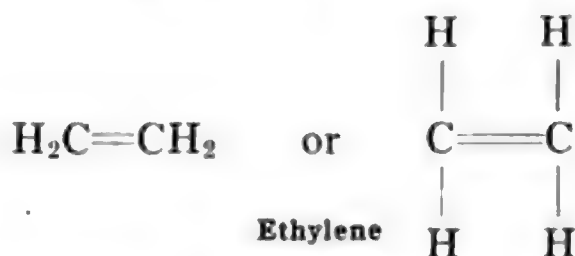
Ethane
 $\text{H}_3\text{C—CH}_3$



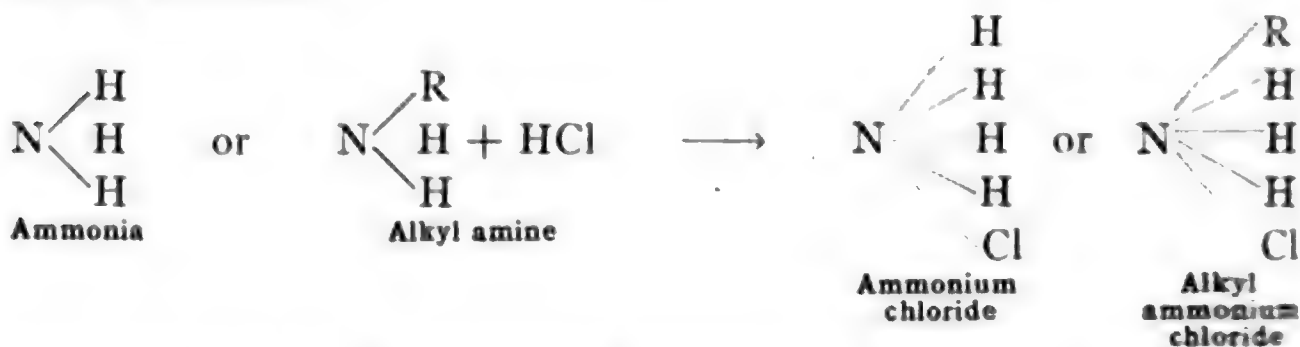
Ethylene
 $\text{H}_2\text{C}=\text{CH}_2$

FIG. 2.

Therefore, in accordance with the facts, viz., (a) *unsaturation and instability of ethylene*. (b) *The formation of ethylene from ethyl alcohol by loss of water*. (c) *The formation of ethylene from ethyl bromide, or iodide, by loss of hydrogen bromide, or iodide*. (d) *The identity of the di-brom addition product of ethylene (ethylene bromide), with the symmetrical di-brom ethane* and, (e) *in accordance with our conceptions of carbon in its space relations and the geometric condition of such space arrangement, the structural formula for ethylene* has been accepted as follows:

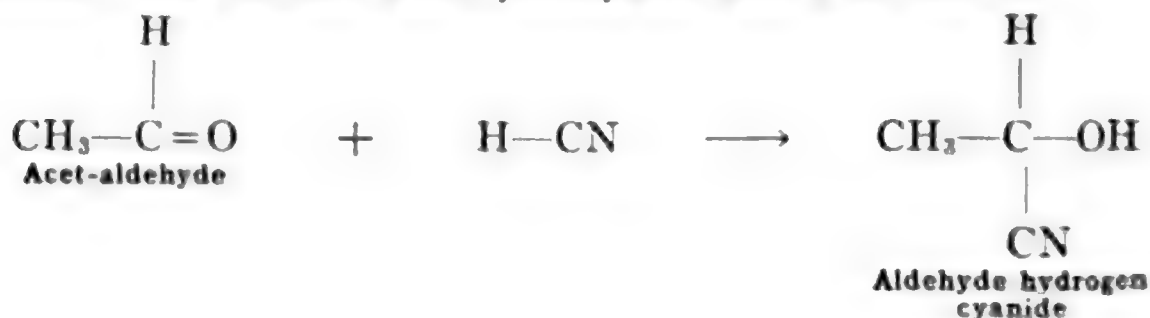


Other Types of Addition.—It may be well to consider two distinctly different cases of seeming unsaturation as indicated by the formation of addition products. When ammonia gas, or ammonia substitution products, viz., the alkyl amines, react with any acid, e.g., hydrochloric acid, addition takes place and the reaction is represented as follows:



In this case the addition of hydrochloric acid is due to, or produces, a *change in the valence of the nitrogen from three in ammonia to five in the ammonium salts*. Here, then, there is *no unsaturation* present.

Another example is that of acetaldehyde, $\text{CH}_3\text{—CHO}$. This compound as it will be recalled, (p. 116) forms addition products with several substances, e.g., hydrocyanic acid, ammonia and sodium acid sulphite. The reaction with hydrocyanic acid is as follows:



In these cases the *character of the grouping is changed* by the conversion of a doubly linked carbonyl oxygen into a singly linked hydroxyl group by means of the hydrogen of the reagent. The other part of the reagent becomes linked to the carbonyl carbon by the new free valence of the latter. In none of the cases is there either *change of valence or unsaturation*. Other similar cases could be mentioned but these will suffice to show how, in the case of ethylene, addition reactions prove unsaturation, while, in the cases of ammonia and acetaldehyde, the formation of addition products is explained in other ways.

A. ETHYLENE OR ETHENE UNSATURATED SERIES

Saturated Hydrocarbons

Methane Series



Ethane CH_3-CH_3

Propane $CH_3-CH_2-CH_3$

Butane $CH_3-CH_2-CH_2-CH_3$

Unsaturated Hydrocarbons

Ethylene Series



Ethylene or Ethene B.P. -103°



Propylene or Propene B.P. 48°

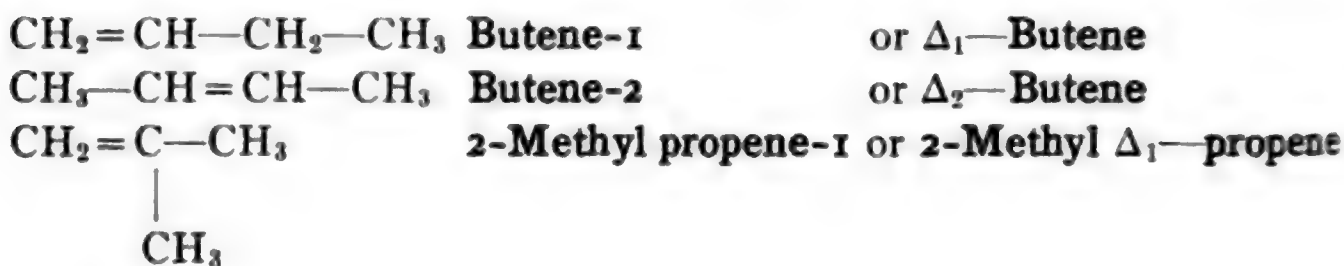


Butylene or Butene-1 B.P. -5°

Homologous Series.—Just as there is a series of hydrocarbons homologous to methane each member of which differs in composition from the preceding one by CH_2 so likewise there is an homologous series of hydrocarbons of which the first member is ethylene. The members of this series bear exactly the same relation to each other as do those of the methane series, *i.e.*, each is the methyl substitution product of the preceding member. Each contains one ethylene group of two carbons linked by a double bond and is related to the corresponding member of the saturated series just as ethylene is to ethane. The general formula for the series is C_nH_{2n} .

Isomers.—The number of possible isomers in the ethylene series is greater than in the saturated series as isomerism may be due not only to the *character of the chain of carbons* but also to the *position of the*

double bond in this chain. The systematic names of the ethylene hydrocarbons correspond to those of the saturated series with the termination *ane* of the latter changed to *ene*. The position of the double bond is also indicated by a numerical suffix. A special sign is also often used to indicate the double bond, viz., the capital Greek letter delta, Δ . Such cases of isomerism and also the names of the compounds may be illustrated by the hydrocarbons of the composition C_4H_8 , as follows:

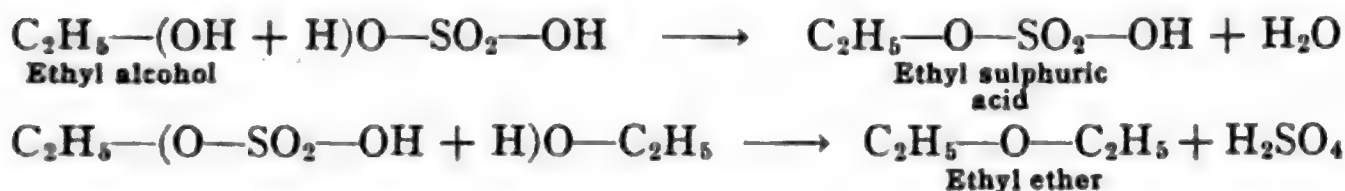


Chemical Properties.—The chemical properties of the ethylene hydrocarbons are, in all cases, like those of ethylene itself. They are more unstable than the corresponding members of the saturated series. This instability is especially shown by their tendency to form addition products by taking up directly, without substitution, *two and only two* halogen atoms and forming, thereby, the di-halogen substitution products of the corresponding saturated hydrocarbon. Not only do the unsaturated hydrocarbons form these addition products with the halogens, but, in some cases, with hydrogen itself, thereby being converted into the corresponding saturated hydrocarbon. With the halogen binary acids the mono-halogen alkyls are formed. With water the unsaturated hydrocarbons yield the saturated hydroxy compounds or alcohols. The ethylene hydrocarbons are oxidizable with potassium permanganate or chromic acid, but yield, by such oxidation, acids poorer in carbon than the hydrocarbon. In this case the ethylene group, the double linked carbons, is destroyed yielding carbon di-oxide. When heated they are all liable to decompose and polymerize.

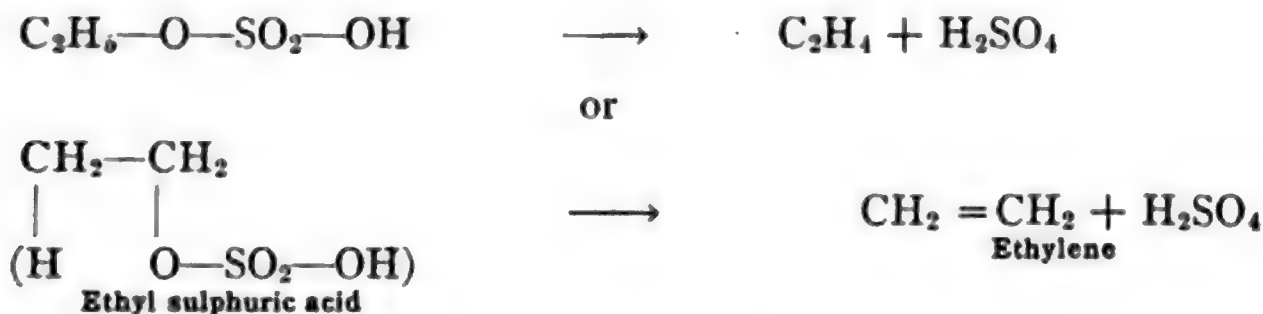
Ethylene $CH_2 = CH_2$ Ethene

The only member of this series to be considered in detail is the first member **ethylene** or **ethene**, C_2H_4 or $CH_2 = CH_2$. It is most readily prepared by heating ethyl alcohol with an excess of sulphuric acid. In the preparation of ethyl ether equal molecular parts of ethyl alcohol

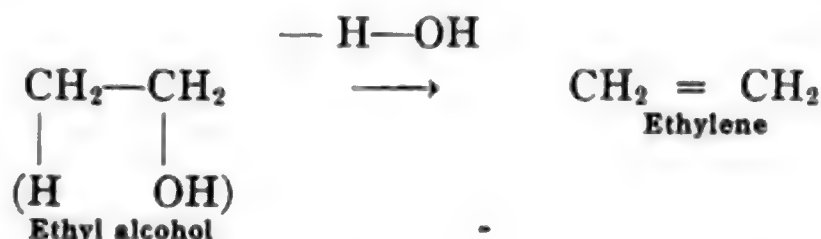
and sulphuric acid are heated to 140° and then more alcohol is added, ether being produced. The reactions taking place are as follows:



If, however, double molecular proportions of sulphuric acid are used and, at 160° , additional sulphuric acid and alcohol are added, the first reaction above is the same then, with the excess sulphuric acid, the ethyl sulphuric acid yields ethylene and sulphuric acid is regenerated, as follows:



In effect, the reaction is simply the *loss of water from one molecule of alcohol*, viz.,

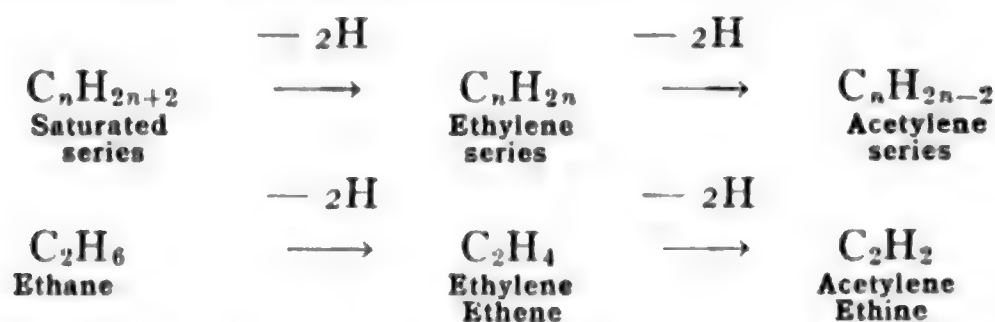


Ethylene is a colorless gas that burns with a smoky flame. It boils at -103° (750 m.m.) and is liquefied at -1.1° at 42 atmospheres pressure. When heated it decomposes and polymerizes yielding various products, *e.g.*, CH_4 , C_2H_6 , C_6H_6 , etc. It is commonly known as *olefiant gas* and is obtained when numerous organic substances are heated. It forms explosive mixtures with oxygen.

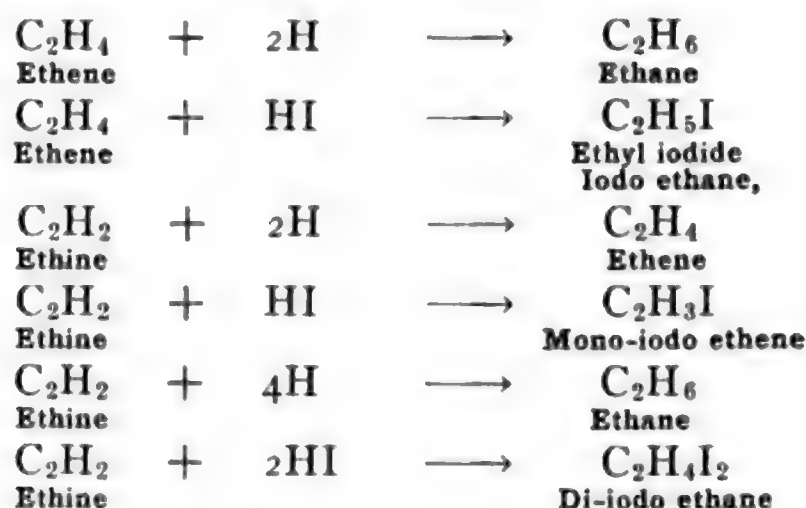
B. ACETYLENE OR ETHINE UNSATURATED SERIES

It has been shown how, by a loss of two hydrogen atoms, the hydrocarbons of the saturated, or methane, series are converted into ethylene unsaturated, or doubly linked compounds. By a further loss of

two hydrogen atoms from the molecule a series of hydrocarbons is obtained possessing still greater unsaturation, as follows:



Just as ethylene, because of its unsaturation, readily takes up *two* mono-valent atoms, forming addition products, and thereby passing over to the saturated series, so it has been found that acetylene, or ethine, readily takes up, by addition, either *two* or *four* mono-valent atoms. In the first case it passes to the more nearly saturated ethylene series and then to the fully saturated or methane series. This relationship may be shown by the following scheme:



Triple Bond.—The structural formula for acetylene, or ethine, analogous to that of ethene is represented as follows:



That is, in acetylene the two carbon atoms are *triply linked* and this constitution agrees with its reactions, with its unsaturation and with the amount of this unsaturation. It has also been established by a similar series of reaction to those discussed in proving the symmetrical, double bond formula for ethylene. Acetylene may be formed from ethane and its derivatives and also from ethylene and its derivatives by the reverse of the reactions cited above, or analogous ones.

Homologous Series, Names.—The homologous members of the acetylene or ethine series of hydrocarbons are related to each other ex-

actly as are those of the methane and ethylene series, *i.e.*, each hydrocarbon is the methyl substitution product of the one preceding. Each compound also contains one group of two carbons linked by a triple bond. The systematic names take the termination *ine* which in official nomenclature of the aliphatic hydrocarbons always signifies an unsaturated compound with a *triple bond* or *acetylene group* just as *ene* signifies an unsaturated compound with a *double bond* or *ethylene group* and *ane* a saturated compound with only *singly linked carbons*. Considering briefly the relation between the three series of hydrocarbons which have thus far been discussed it may best be shown by the following tabular arrangement of the first four members of each series.

Saturated Hydrocarbons		Unsaturated	Hydrocarbons
<i>Methane Series</i>		<i>Ethylene Series</i>	<i>Acetylene Series</i>
General formula	C_nH_{2n+2}	C_nH_{2n}	C_nH_{2n-2}
C_2	C_2H_6 CH_3-CH_3 Ethane	C_2H_4 $CH_2=CH_2$ Ethene	C_2H_2 $CH \equiv CH$ Ethine
C_3	C_3H_8 $CH_3-CH_2-CH_3$ Propane	C_3H_6 $CH_3=CH-CH_3$ Propene	C_3H_4 $CH \equiv C-CH_3$ Propine
C_4	C_4H_{10} $CH_3-CH_2-CH_2-CH_3$ Butane	C_4H_8 $CH_3=CH-CH_2-CH_3$ Butene-1 $CH_3-CH=CH-CH_3$ Butene-2	C_4H_6 $CH \equiv C-CH_2-CH_3$ Butine-1 $CH_3-C \equiv C-CH_3$ Butine-2
	$CH_3-CH-CH_3$ CH_3 2-Methyl propane	$CH_3=C-CH_3$ CH_3 2-Methyl propene	

These three series include all of the more common hydrocarbons belonging to what are termed *open chain* or *a-cyclic* (non-cyclic) compounds. Furthermore, almost all of the derived compounds here studied are derivatives of hydrocarbons belonging to one of these series.

Acetylene $CH \equiv CH$ Ethine

This hydrocarbon is the first member and gives its name to the series. It was discovered by **Davy** in 1836 and was synthesized from the elements and its constitution established by **Berthelot** in 1859. It is formed when organic compounds are incompletely oxidized, as when a **Bunsen** burner *strikes back* and gives off a gas with a characteristic

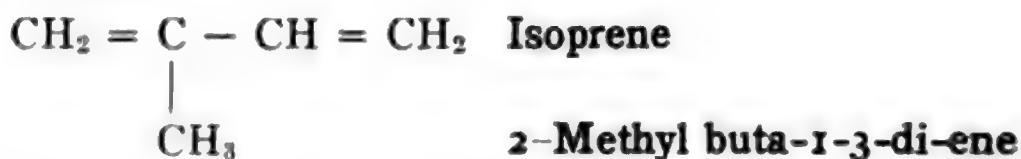
odor. It is a colorless gas that burns with a brilliant flame giving a very satisfactory light. It is often used for illumination purposes with specially designed lamps or in connection with small generators. For this purpose it is made from calcium carbide, CaC_2 , by the action of water.



An important property of acetylene is the ease with which it forms metallic compounds especially with copper and with silver. These compounds are explosive both by heat and by detonation. In many of the explosive accidents in connection with acetylene gas plants the cause has been the formation of these metallic compounds.

C. DI-ETHYLENE HYDROCARBONS—DI-ENES

Isoprene.—Isomeric with the acetylene series of hydrocarbons are those which contain not one but *two sets of doubly linked carbon atoms*. As each additional bond between carbons means the loss of two hydrogen atoms, then two double bonds and one triple bond will be equivalent and will represent a loss of *four* hydrogen atoms from the saturated hydrocarbon. Therefore the general formula is $\text{C}_n\text{H}_{2n-2}$. Hydrocarbons containing two pairs of doubly linked carbons or ethylene groups are termed **di-ethylenes** or **di-enes**. The only compound to be mentioned contains five carbons, and is known as **isoprene**, C_5H_8 . Its constitution has been established as a four carbon chain with a substituting methyl linked to carbon 2 and with double bonds at carbons 1 and 3, as follows:

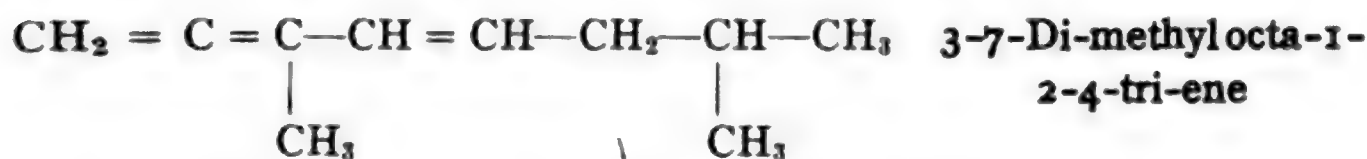


Isoprene is of especial importance in connection with the terpenes as it has been shown to be the mother hydrocarbon of **caoutchouc** or **rubber**. Its constitution and properties will be discussed again later on.

D. HYDROCARBONS OF GREATER UNSATURATION

While most of the compounds commonly met with are derivatives of one of the three series of hydrocarbons which have been studied it should be mentioned that hydrocarbons are known which possess still

greater unsaturation than exists in those of the general formulas C_nH_{2n} and C_nH_{2n-2} . As the loss in hydrogen is by twos, compounds of greater unsaturation would be expressed by the formulas C_nH_{2n-4} , C_nH_{2n-6} , etc. Considering the formulas for ethylene and acetylene, viz., $CH_2 = CH_2$ and $CH \equiv CH$, we see that a hydrocarbon of two carbon atoms cannot exist with unsaturation beyond C_nH_{2n-2} , as in the case of acetylene. The loss of two more hydrogen atoms from it would leave simply elemental carbon. It is plain, therefore, that the only way in which greater unsaturation can result is by increasing the number of doubly or triply linked groups. As in the case of isoprene, two doubly linked groups are equivalent to one triply linked group so a compound of the formula C_nH_{2n-4} must contain *three doubly linked groups*, and one of the composition C_nH_{2n-6} may have *two triply linked groups*. Only one hydrocarbon of each of these highly unsaturated series will be mentioned. The one of the composition C_nH_{2n-4} has the empirical formula $C_{10}H_{16}$ and is important because it is isomeric with the **terpenes** (Pt. II). Its constitution has been established as an eight carbon chain with two methyl groups substituted in carbons 3 and 7 and with three double bonds at carbons 1, 2 and 4. It is thus a *tri-ene*. Its formula and systematic name are, therefore,



Di-propargyl.—The hydrocarbon with the general formula C_nH_{2n-6} has the composition C_6H_6 and is known as **di-propargyl**. It has been shown to contain *two triple bonds* and is thus a *di-ine*. Its constitution has been established as a straight chain of six carbons with the triple bonds at carbons 1 and 5. Its formula is

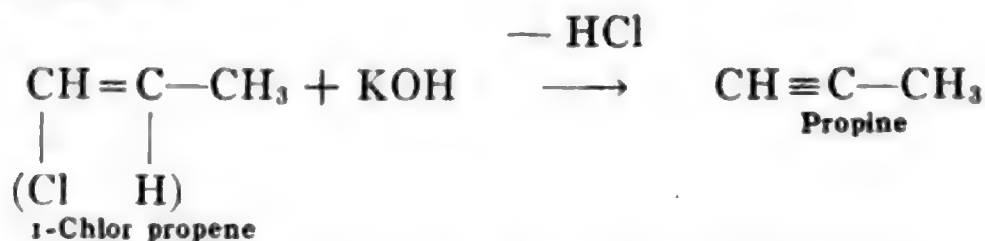


It is known as **di-propargyl** because the group $(CH \equiv C - CH_2 -)$ is called **propargyl** (p. 167). The compound is of importance because it is isomeric with **benzene** which is a *cyclic* or *closed chain* hydrocarbon and the mother substance of a large series of compounds constituting Part II of this book.

V. MONO-SUBSTITUTION PRODUCTS OF UNSATURATED HYDROCARBONS

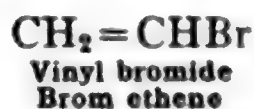
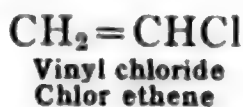
A. HALOGEN AND CYANOGEN SUBSTITUTION PRODUCTS

The mono-halogen substitution products of the ethylene series of hydrocarbons are of two classes. These may be best illustrated with the hydrocarbon propene, $\text{CH}_2=\text{CH}-\text{CH}_3$. In such a hydrocarbon containing a double bond, substitution may take place either in a carbon which is not doubly linked or in one of the two which is doubly linked. In the former case, as in the compound $\text{CH}_2=\text{CH}-\text{CH}_2\text{Cl}$, **3-chlor propene**, the compound resulting is a true analogue of the substitution products of the saturated hydrocarbons. The chlor propene above is *like* the alkyl halides and as such yields alcohols, amines, cyanides, etc., when treated with silver hydroxide or potassium hydroxide, with ammonia or with potassium cyanide. When, however, a halogen is substituted in one of the carbons which is doubly linked as in $\text{CHCl}=\text{CH}-\text{CH}_3$, **1-chlor propene**, or $\text{CH}_2=\text{CCl}-\text{CH}_3$, **2-chlor propene**, then the compound is *not like* the alkyl halides and does not yield an alcohol, amine or cyanide as in the former case. When such a halide is treated with potassium hydroxide it loses the halogen and one hydrogen and is converted into a hydrocarbon of the ethine series, as follows:



VINYL HALIDES—HALOGEN ETHENES

Vinyl Chloride.—As ethylene or ethene contains doubly linked carbons only, substitution of halogen will result in a compound of the second class given above.

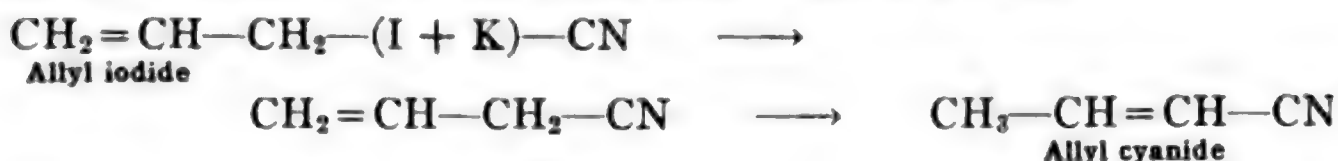


The radical ($\text{CH}_2=\text{CH}-$) is known as **vinyl**.

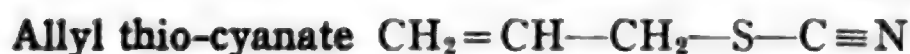
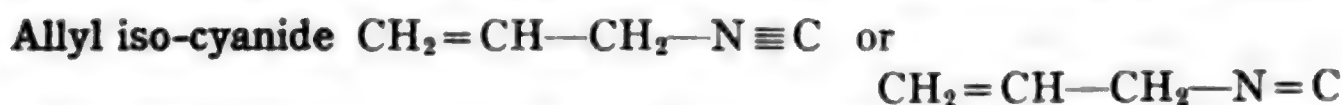
ALLYL HALIDES, CYANIDES, ETC.

Allyl Chloride.—The halogen substitution products of propene and the higher hydrocarbons of the ethene series, when the substitution is in a carbon group not doubly linked, are of importance in the synthesis of derivatives in the same way as are the alkyl halides. **3-Chlorpropene** or **propenyl chloride**, $\text{CH}_2=\text{CH}-\text{CH}_2\text{Cl}$, is known also as **allyl chloride**, the radical ($\text{CH}_2=\text{CH}-\text{CH}_2-$) being known as **allyl**.

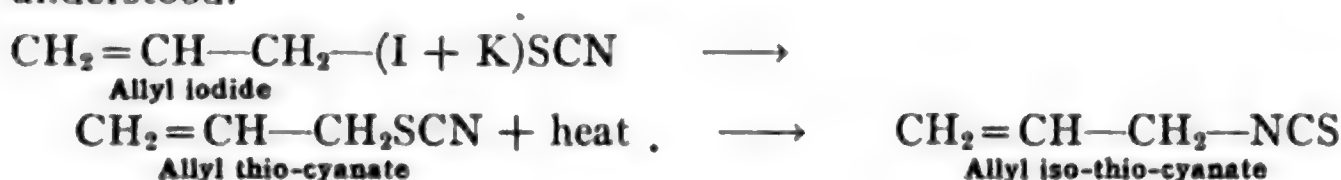
Allyl Cyanide, Iso-thio-cyanate, etc.—From allyl chloride or the iodide there may be prepared by the customary reactions **allyl cyanide** and other of the cyanogen compounds. With potassium cyanide allyl iodide yields **allyl cyanide**. The reaction, however, instead of yielding a cyanide of the expected constitution is accompanied by a shifting of the double bond to the second carbon so that the cyanide has a constitution unlike that of the iodide from which it is made.



This is proven by the fact that allyl cyanide on hydrolysis yields **crotonic acid** in which the double bond is at carbon-2 (p. 173). Of the other cyanogen derivatives of propene the following are known though the position of the double bond is not established in all cases.



Oil of Mustard.—Only the last compound named is important, viz., **allyl iso-thio-cyanate**, $\text{CH}_2=\text{CH}-\text{CH}_2\text{NCS}$. Strange as it may seem, from statements made in connection with the cyanates and iso-cyanates of the saturated series, this compound is made by treating allyl-iodide, not with silver thio-cyanate, but with potassium thio-cyanate. As, however, the tautomeric iso-compounds are made from the cyanates and thio-cyanates by heat, the conversion of the first formed thio-cyanate into the iso-thio-cyanate can readily be understood.



Allyl iso-thio-cyanate is found in nature as a glucoside constituent of mustard seed. It is known, therefore, as *mustard oil*. It is a liquid with a sharp odor and with a boiling point of 150.7° . The proof that it is iso-thio-cyanate is its conversion into **allyl-amine**, $\text{CH}_2 = \text{CH}-\text{CH}_2\text{NH}_2$.

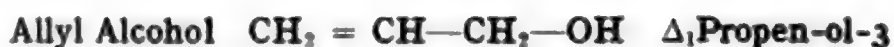
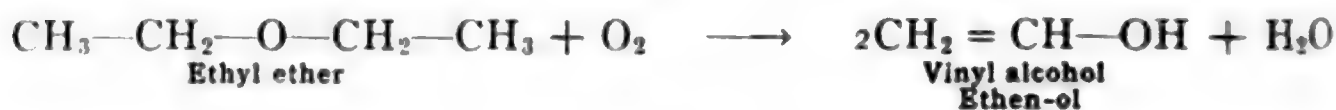
B. UNSATURATED ALCOHOLS

I. ETHYLENE SERIES $(\text{C}_n\text{H}_{2n-1})-\text{OH}$

As primary alcohols must contain the group $(-\text{CH}_2-\text{OH})$, it is plain that the simplest primary alcohol of the ethylene hydrocarbons must be derived from the first hydrocarbon of this series which contains a methyl group. This will be the three carbon member, viz., propene, $\text{CH}_2 = \text{CH}-\text{CH}_3$. As ethene, $\text{CH}_2 = \text{CH}_2$, contains no such methyl group it can not yield a primary alcohol.



The only hydroxyl substitution product of ethene which is possible, and the only one known, has the constitution represented by the above formula and is plainly a secondary alcohol as it contains the secondary group $(=\text{CH}-\text{OH})$. It may be produced by the oxidation of ethyl ether by means of chromic acid, CrO_3 , ozone, or even by air when in the sunlight.

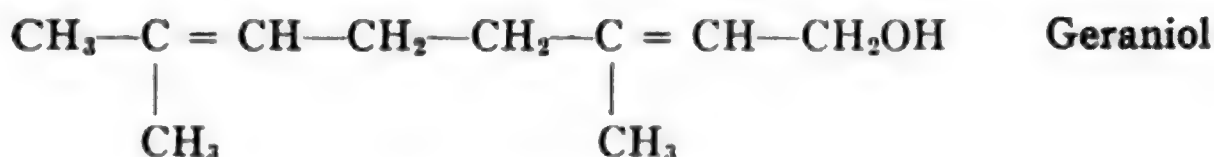


This simplest primary alcohol of the ethylene series, and commonly known as **allyl alcohol**, is produced from glycerol (glycerin) by a reaction which will be discussed later. It is also produced by the destructive distillation of many organic substances, such as wood, and is therefore found as a constituent of crude wood alcohol. It is a colorless liquid with a strong odor and it boils at 96.6° . It mixes in all proportions with water. By the action of nascent hydrogen, $\text{Zn} + \text{H}_2\text{SO}_4$, it is converted into the corresponding saturated alcohol:



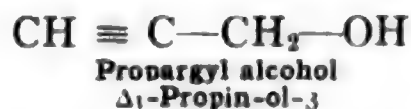
Higher Ethylene Alcohols

Geraniol.—Alcohols derived from higher hydrocarbons of the ethylene series are known. The most important one is derived from a *di-ene* containing ten carbons and belongs to a class of compounds known as *terpenes* which will be considered later (Pt. II). It is called **geraniol** and has the following constitution.



II. ACETYLENE SERIES ($\text{C}_n\text{H}_{2n-2}$)—OH

Propargyl Alcohol.—Only one alcohol of this series will be considered. The simplest primary alcohol possible derived from hydrocarbons of the acetylene series is the one derived from **allylene**, $\text{CH} \equiv \text{C}-\text{CH}_3$, **methyl acetylene**.



We have referred to this alcohol (p. 163) in connection with the unsaturated di-ene hydrocarbon **1-5-hexa-di-ene**, $\text{CH} \equiv \text{C}-\text{CH}_2-\text{CH}_2-\text{C} \equiv \text{CH}$, which is known as **di-propargyl** because it contains two of the groups present in the above alcohol, *i.e.*, the *propargyl radical* ($\text{CH} \equiv \text{C}-\text{CH}_2-$).

C. ETHERS AND THIO-ETHERS

Thio-ethers.—**Ethers** derived from the unsaturated hydrocarbons are known but are not important. The corresponding sulphur compounds, *viz.*, the **thio-ethers**, are, however, of considerable importance and are represented by a commonly occurring substance. The thio-ether related to allyl alcohol is known as **allyl thio-ether**, or, also as **allyl sulphide**. It is made, like the thio-ethers of the saturated series, by treating the iodide of the hydrocarbon with potassium sulphide.



Oil of Garlic.—This compound, usually known by the latter name, **allyl sulphide**, is a constituent of *oil of garlic* and is a liquid with an odor resembling that of garlic.

D. UNSATURATED ALDEHYDES

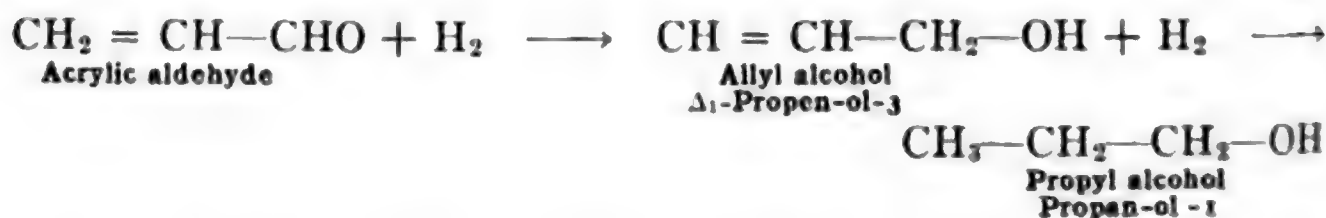
The aldehydes of the ethylene series which result from the alcohols by oxidation, and the acids which are the oxidation products of the aldehydes, both contain several important naturally occurring members.

Acrylic Aldehyde $\text{CH}_2 = \text{CH}-\text{CHO}$ **Acrolein**

When allyl alcohol, Δ_1 -propen-ol-3, is oxidized carefully **allyl aldehyde** is obtained. As this aldehyde yields **acrylic acid** on further oxidation it is more commonly known as **acrylic aldehyde** and also as **acrolein**.



We have mentioned the fact that allyl alcohol is formed from glycerol, the reaction for which will be considered later. Similarly, allyl aldehyde, or acrylic aldehyde, is obtained when glycerol is heated. Fats being glycerol derivatives, as we shall see when we study this compound, they, too, on heating yield acrylic aldehyde. It is a volatile liquid boiling at 52.4° , with a sharp odor which is very penetrating and which acts upon the eyes causing the flow of tears. Hence, when fats or glycerol are strongly heated a sharp odor is noticed due to the formation of acrylic aldehyde. The aldehyde on reduction with hydrogen yields, first, **allyl alcohol** which, on further action of hydrogen, yields **propyl alcohol**.



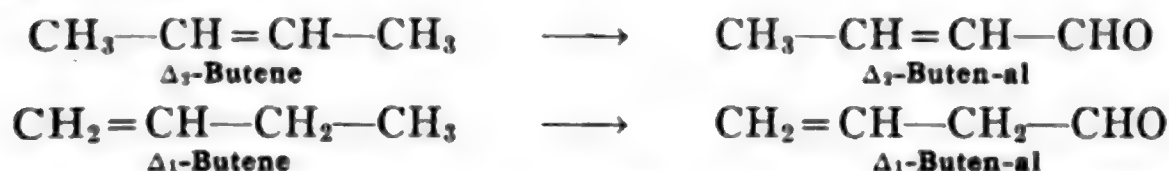
Similarly, on addition of hydrochloric acid, the aldehyde yields **chlorpropionic aldehyde**, or **3-chlor-propan-al**.



Thus the unsaturated character of the hydrocarbon chain and the presence of the aldehyde group are both proven. As an aldehyde, it also forms addition products with ammonia, hydrogen cyanide and sodium acid sulphite.

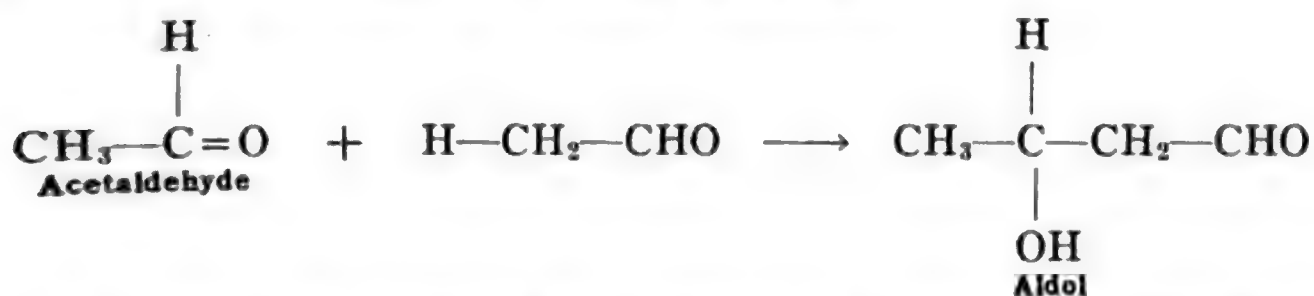
Crotonic Aldehyde $\text{CH}_3\text{—CH=CH—CHO}$ $\Delta_2\text{-Buten-al}$

The aldehyde derived from the next higher hydrocarbon of the ethylene series, viz., the four carbon hydrocarbon, **butene**, is known as **crotonic aldehyde** because on oxidation it yields an acid known as **crotonic acid**. As there are two isomeric butenes due to the position of the double bond there will likewise be possible two isomeric aldehydes or butenals.

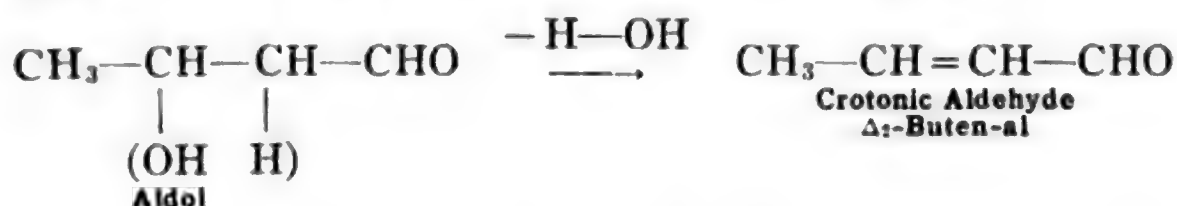


Now the aldehyde which yields **crotonic acid** on oxidation, *i.e.*, **crotonic aldehyde**, may be prepared by a synthesis which shows clearly that it must have the constitution of the first of these isomeric aldehydes, $\Delta_2\text{-buten-al}$, $\text{CH}_3\text{—CH=CH—CHO}$.

Aldol Condensation.—In discussing the addition products formed from acetaldehyde (p. 116), it was stated that it forms a condensation product with a second molecule of itself. The product is **aldol**, the reaction being known as the *aldol condensation*.

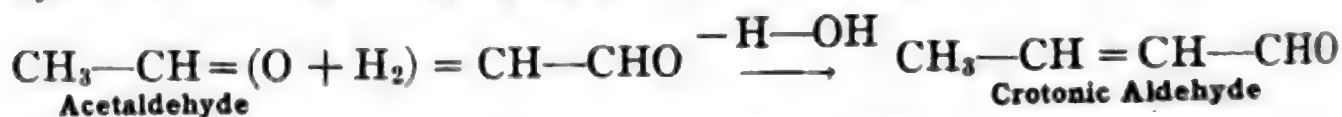


Now aldol readily loses water yielding an unsaturated aldehyde just as ethyl alcohol by loss of water yields ethylene (p. 154).



In this reaction which may apparently be brought about in one step, though aldol is undoubtedly an intermediate product even when it is

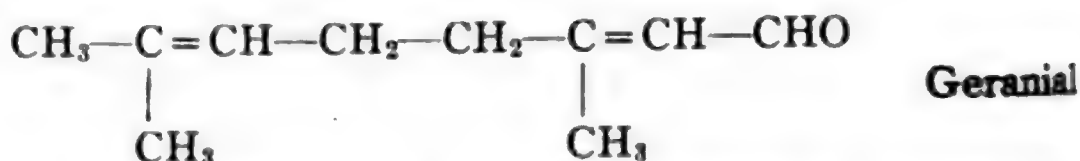
not isolated, it has been definitely shown that the *two atoms of hydrogen* which go to make up the molecule of water which is lost *both come from the methyl group of the second acetaldehyde molecule*. This establishes the double bond in crotonic aldehyde as between the *second and third* carbon groups as in Δ_2 -**buten-al**. The condensation of acetaldehyde to crotonic aldehyde as one reaction may be written therefore,



Other reactions support this constitution for crotonic aldehyde.

Higher Ethene Aldehydes

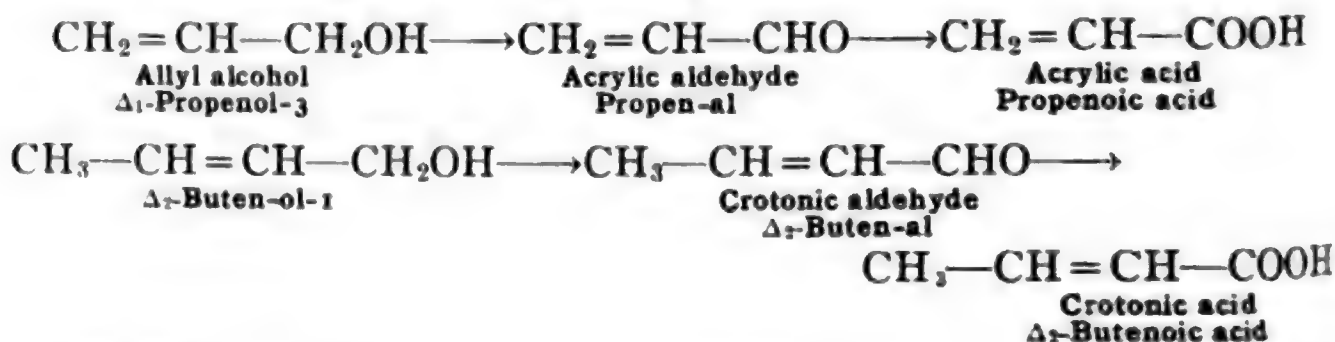
Geranial.—Corresponding to the higher ethene alcohol **geraniol** (p. 167) is the aldehyde derived from it and known as **geranial**. It has the constitution



This compound and a related one known as **citronellal** belong with **geraniol** in the class of **terpenes** and will be considered in Part II.

E. UNSATURATED ACIDS

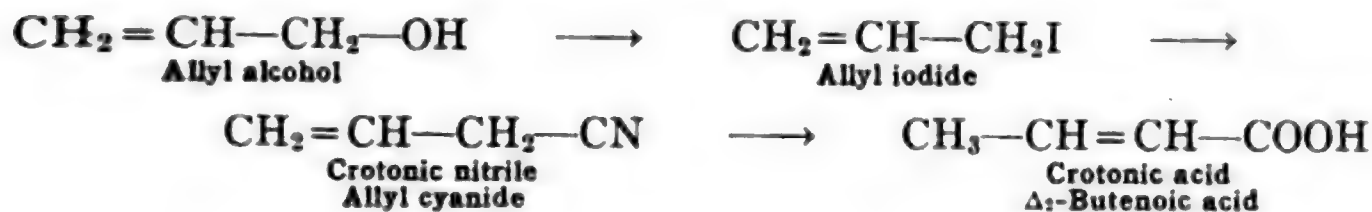
Just as the saturated primary alcohols on oxidation yield first aldehydes and then acids so the ethylene unsaturated primary alcohols yield first the unsaturated aldehydes, just considered, and these on further oxidation yield corresponding unsaturated acids,



Synthesis.—The synthetical preparation of these ethylene unsaturated acids may be accomplished by the same general reactions as those used in the preparation of the saturated acids.

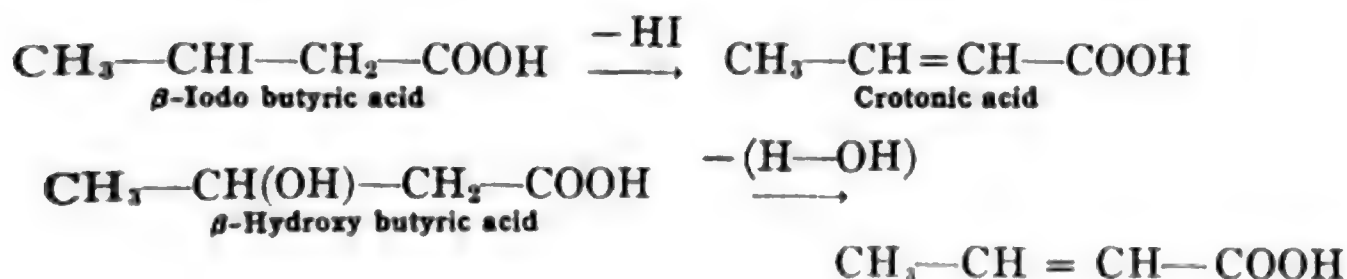
(1) *By the oxidation of the unsaturated aldehyde*; as in the reactions above.

(2) *From the unsaturated alcohols, or the halogen substitution products, by conversion, first, into the corresponding cyanide, or acid nitrile, and the hydrolysis of this to the acid containing one more carbon than the original alcohol or halogen compound.*

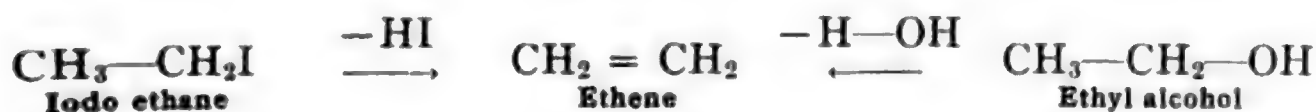


In this series of reactions there occurs a *shifting of the double bond* from the first to the second carbon atom either in the allyl cyanide or when this is hydrolyzed to the acid for the acid obtained is **crotonic acid** which as we shall see has the constitution of Δ_2 -butenoic acid.

(3) *From the corresponding saturated acid, which contains in the second carbon group from the carboxyl, i.e., the beta position, either a substituted halogen atom, or, a hydroxyl group.*



These syntheses are similar to those of ethylene from iodo ethane by the loss of hydrogen iodide and from ethyl alcohol by the loss of water.

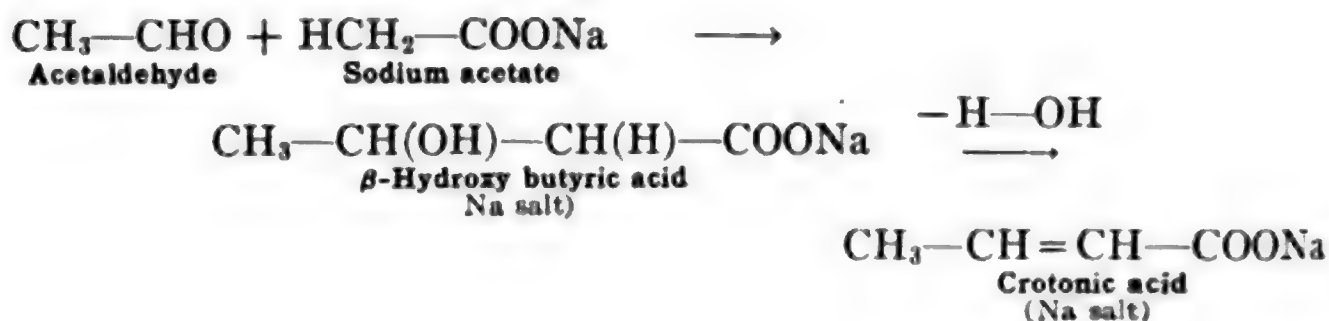


They are also similar to the one referred to in the formation of crotonic aldehyde from β -hydroxy butenal.

(4) Another general method of synthesis of unsaturated acids from saturated compounds involves this same reaction as a second step.

Perkin-Fittig Synthesis.—The first step in the synthesis is analogous to the *aldol condensation*. It consists in the addition of a sodium salt of an acid, usually acetic acid, to a saturated aldehyde, whereby condensation is effected and a *beta*-hydroxy acid is formed. The *beta*-

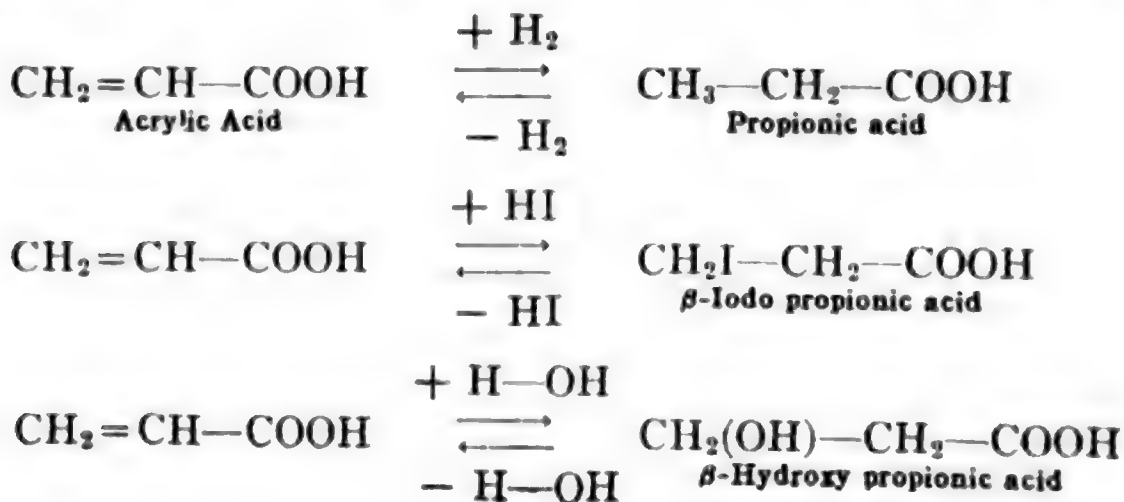
hydroxy acid is then converted into the unsaturated acid in the same way as in (3).



This is the simplest case of the reaction but it has been mostly used in the synthesis of higher members of the unsaturated acid series, *e.g.*, the nine carbon acid, **nonylenic acid**, which is prepared from the seven carbon aldehyde known as **œnanthylic aldehyde**, or **œnanthol**, obtained from *castor oil*. Even more important than its application in the synthesis of higher acids of the ethylene series is the use of the reaction in the synthesis of *aromatic unsaturated acids derived from benzene* and containing an unsaturated side chain (see **cinnamic acid**, Part II). The reaction is known as the **Perkin Synthesis** or as the **Perkin-Fittig Synthesis** from the men who suggested and explained it.



The first member of the *ethylene series of acids*, viz., **propen-oic acid**, or as it is commonly known, **acrylic acid**, is a sharp smelling liquid which boils at 140° and melts at 7°. It readily forms addition products. With hydrogen it yields propionic acid; with hydrogen iodide, β -iodo propionic acid and with water, β -hydroxy propionic acid. This last acid, which we will consider later (p. 245), because of this relation to acrylic acid, is also known as **hydracrylic acid**. From these compounds just mentioned acrylic acid may be formed by the loss of the same elements.



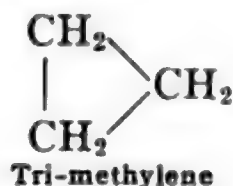
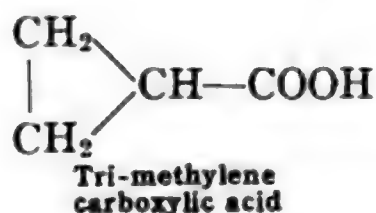
Other methods of preparing **acrylic acid** are by the oxidation of the corresponding unsaturated alcohol or aldehyde, viz., **allyl alcohol**, $\text{CH}_2=\text{CH}-\text{CH}_2-\text{OH}$, and **acrylic aldehyde**, $\text{CH}_2=\text{CH}-\text{CHO}$.

Crotonic Acid $\text{CH}_3-\text{CH}=\text{CH}-\text{COOH}$ Δ_2 -**Butenoic Acid**

The second acid of the ethylene unsaturated series, viz., one containing four carbon atoms, therefore a derivative of butene and systematically named butenoic acid, is a naturally occurring substance known as **crotonic acid**. We have mentioned the fact that the existence of the double bond, in compounds containing more than three carbon groups in the chain, increases the possibility of isomerism because of the different position which the double bond may occupy. Butenoic acid, as it contains one double bond, or ethene group, may, according to the different position which the double bond may occupy, and also because of the different position which the methyl group may occupy, exist in all of the following forms:

- (A) $\text{CH}_3-\text{CH}=\text{CH}-\text{COOH}$ Δ_2 -**Butenoic acid**
- (B) $\text{CH}_2=\text{C}(\text{CH}_3)-\text{COOH}$ 2-**Methyl propenoic acid**
- (C) $\text{CH}_2=\text{CH}-\text{CH}_2-\text{COOH}$ Δ_1 -**Butenoic acid**

Also, a fourth possibility exists for an acid of the composition, $\text{C}_3\text{H}_5-\text{COOH}$, which, however, has an entirely different constitution, viz.,



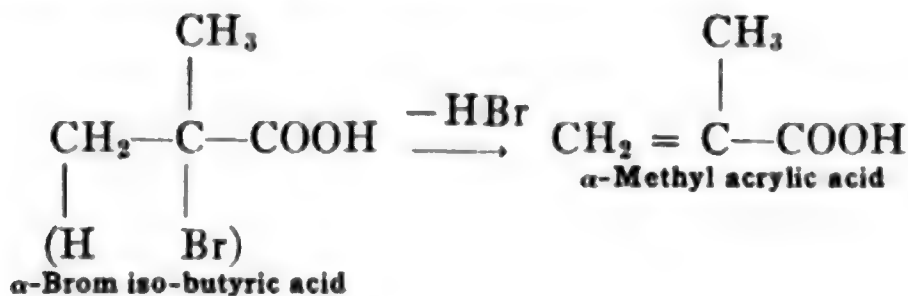
Such an acid is known but it is not an unsaturated compound. It is what is termed a *cyclic compound* derived from a hydrocarbon known as **tri-methylene**, and also as **cyclo propane** (Pt. II). The acid is thus known as **tri-methylene carboxylic acid** and also as **cyclo propanoic acid**.

Let us consider then only those acids of the composition $\text{C}_3\text{H}_5-\text{COOH}$ which contain a double bond or ethene group and the possible constitutions of which we have represented above by the formulas (A),

(B), and (C). Now the fact is that not three acids only but *four* are known which correspond to the three possible constitutions. How then are these facts harmonized? The four known acids are

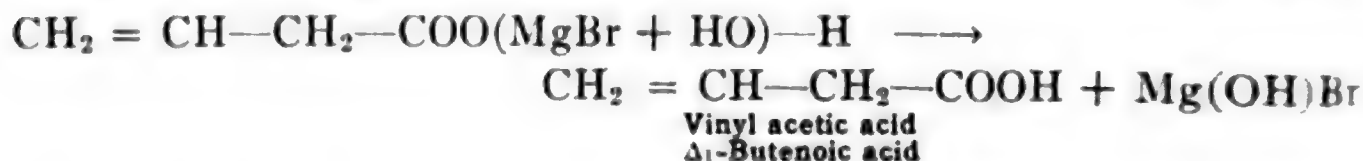
		m.p.	b.p.
Crotonic acid,	a solid	71°	180°
Iso-crotonic acid,	a liquid	15°	172°
Methyl acrylic acid,	a solid	16°	160°
Vinyl acetic acid,	a liquid		168°

***alpha*-Methyl Acrylic Acid.**—The third acid **methyl acrylic acid** may be synthesized from ***alpha*-brom iso-butyric acid**, or **2-brom 2-methyl propanoic acid**, by loss of hydrobromic acid with potassium hydroxide just as acrylic acid is made from ***beta*-brom propionic acid**.



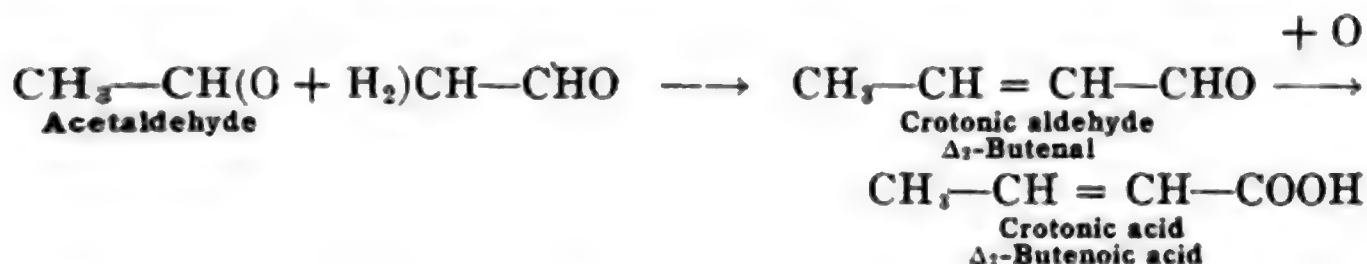
This synthesis proves it to be the *alpha*-methyl acrylic acid corresponding to formula (B). That is, **2-methyl propanoic acid**.

Vinyl Acetic Acid.—**Vinyl acetic acid** may be synthesized from **allyl bromide** by means of the **Grignard reaction** which introduces the carboxyl group in place of the halogen. This proves the constitution to be that of **Δ_1 -butenoic acid**.

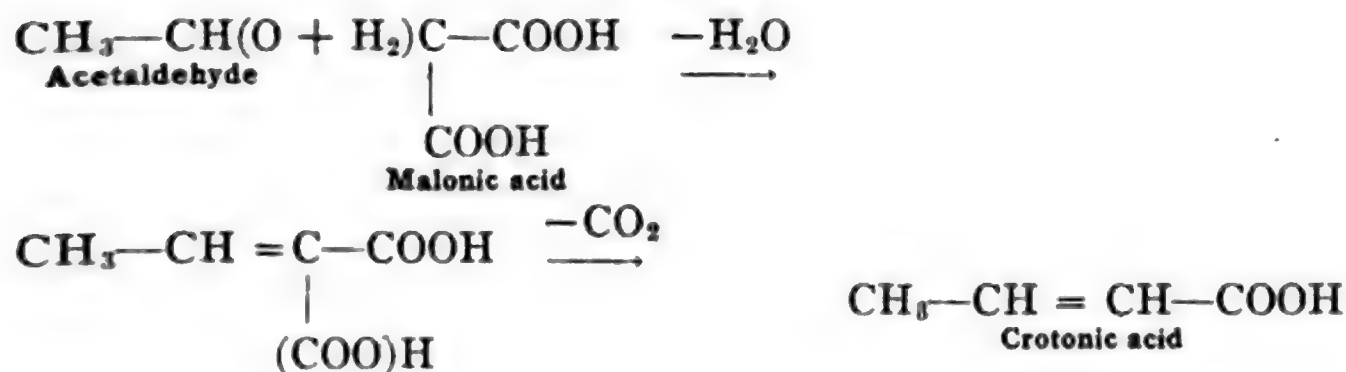


Crotonic and Iso-crotonic Acids.—We have then for the *two* crotonic acids only *one* possible constitution remaining and their synthesis proves that both of these acids do in fact have the *same* structural constitution, viz., that of ***beta*-methyl acrylic acid** or **Δ_2 -butenoic acid**.

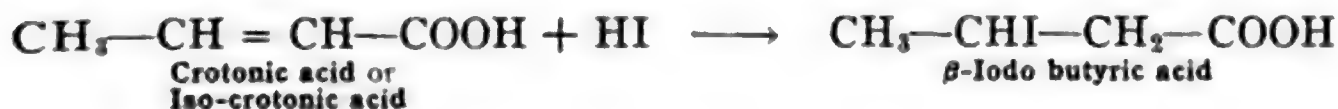
Crotonic Acid from Crotonic Aldehyde.—We have previously shown (p. 169), that crotonic aldehyde is Δ_2 -butenal because of its synthesis by the *aldol condensation* of acetaldehyde. On simple oxidation crotonic aldehyde yields crotonic acid which must therefore have the constitution of Δ_2 -butenoic acid,



From Acetaldehyde and Malonic Acid.—Another synthesis proves the constitution of crotonic acid as Δ_2 -butenoic acid. A di-basic acid known as **malonic acid** has the constitution of *di-carboxy methane*, $\text{HOOC—CH}_2\text{—COOH}$. When this acid is heated with acetaldehyde (paraldehyde) and glacial acetic acid condensation occurs as in the synthesis of crotonic aldehyde and in the **Perkin-Fittig** synthesis (p. 172). A dibasic acid is obtained which loses carbon dioxide and yields a mono-basic acid which is **crotonic acid**.



Now iso-crotonic acid is readily transformed into crotonic acid by simply heating to 170° and crotonic acid may likewise be converted into iso-crotonic acid. Also each of them by the addition of hydrogen iodide is converted into the same saturated compound, viz., β -iodo butyric acid.



Other reactions support the view that these two crotonic acids, which differ sharply in physical properties but closely resemble each other in

their chemical properties, being formed by the same reactions, convertible into the same products and easily transformed into each other, are in fact of *identical structure*, viz., that of **β -methyl acrylic acid** or **Δ_2 -butenoic acid**. We have then the following facts established as to the structural constitution of the four acids we are discussing.

Crotonic acid

and

$\text{CH}_3\text{—CH=CH—COOH}$ **β -Methyl acrylic acid**

Iso-crotonic acid

Δ_2 -Butenoic acid

Methyl acrylic acid $\text{CH}_2 = \text{C}(\text{CH}_3)\text{—COOH}$ **α -Methyl acrylic acid**

2-Methyl propenoic acid

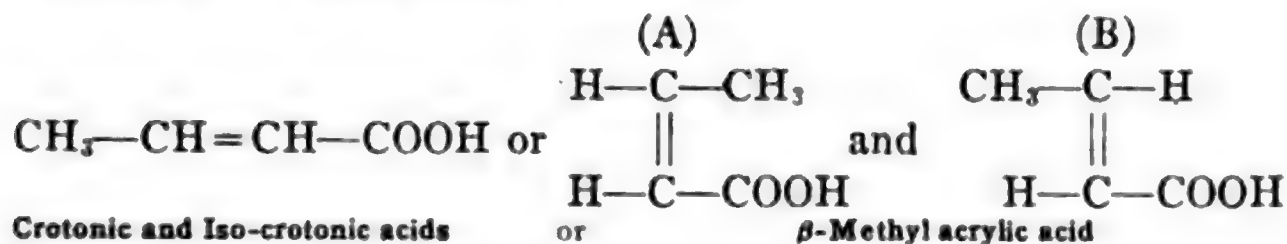
Vinyl acetic acid $\text{CH}_2 = \text{CH—CH}_2\text{—COOH}$ **Δ_1 -Butenoic acid**

Having, then, *two different acids, of the same constitution*, it is necessary to explain their existence and their difference by some theory of isomerism. This brings us to the consideration of a new kind of *space-isomerism*. In connection with active amyl alcohol or 2-methyl butanol-1, we discussed the **van't Hoff-LeBel** theory of the asymmetric carbon atom, by which the existence of three stereoisomeric compounds may be explained. The compounds all have the same structure but differ in the arrangement of the atoms and groups in space around a central asymmetric carbon atom. This carbon atom, because of its union to four different atoms or groups, takes on the property of asymmetry and forms right- and left-handed compounds. According to this theory, carbon is represented as a tetravalent element situated at the center of a regular tetrahedron, with the lines representing its union with other elements directed toward the apexes of the tetrahedron, as shown in Fig. 1, p. 90.

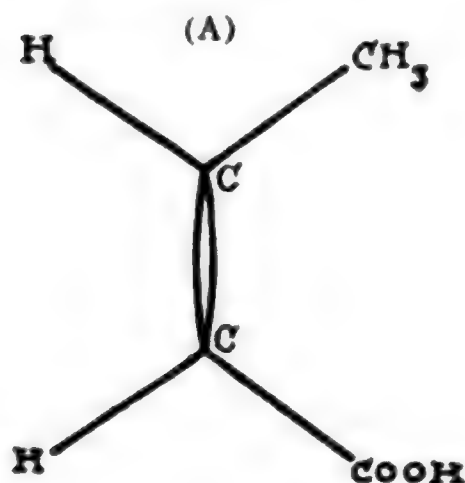
In the case of **tartaric acid**, which we shall study later, we have to consider two such carbon atoms directly united to each other by one of the bonds, and we shall find that the theory applies as truly here as in the first case given of the active amyl alcohols.

Geometric Isomerism.—The theory was applied by **van't Hoff** and **Wislicenus** to the present case of the isomeric **crotonic acids**, and other compounds of similar character, viz., **maleic acid** and **fumaric acid** (p. 290). If two carbon atoms, instead of being linked by one bond, become directly linked by a double bond, as in the case of crotonic acid and iso-crotonic acid, the relation of the two carbon atoms, and of the two groups containing them, becomes *fixed* in space, because the double

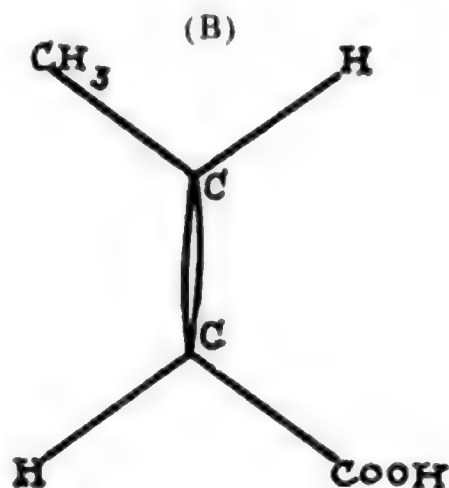
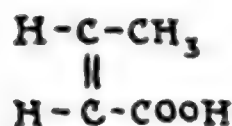
bond *prevents rotation* of these carbon groups. We may write the formulas on a plane surface as follows:



If we represent the formulas by the tetrahedral figures we have the following:



Crotonic acid
cis form



Iso-crotonic acid
trans form

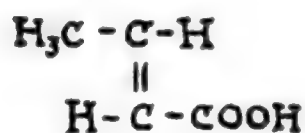
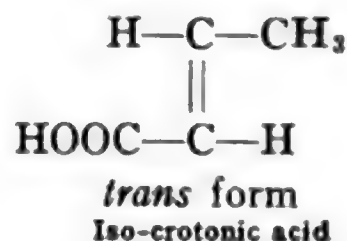
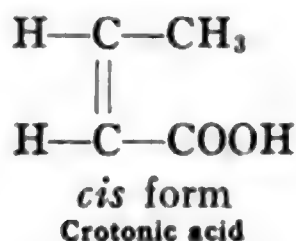


FIG. 3.

As this position is fixed in space isomeric compounds are possible in which the position of two of the elements or groups linked to the doubly bound carbon atoms are reversed, as in (A) and (B) above. Two *stereo-isomeric* compounds should therefore be possible according to such a space arrangement and the two isomeric crotonic acids may thus be explained. This kind of stereo-isomerism is termed *geometric isomerism*. Without taking up in detail the proofs as to which of the two stereo-chemical formulas applies to each of the two crotonic acids, we may simply state the fact, that the properties of the solid or **ordinary crotonic acid** prove that it must be represented by formula (A), above, in which the methyl and carboxyl groups are

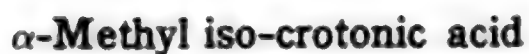
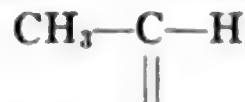
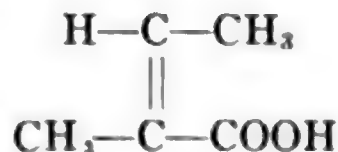
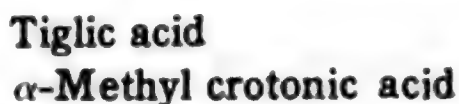
both on the *same* side. Because these two groups are on the same side this particular formula is known as the *cis* form. The other formula, in which these two groups are on opposite sides represents, similarly, the *trans* form. The **iso-crotonic acid** is represented, therefore, by the *trans* formula. The formulas, then, for the two *structurally identical but stereo-isomeric* **β -methyl acrylic acids** or **crotonic acids**, are,



Crotonic acid, the solid, crystallizes from hot water in fine needles which melt at 71° to 72° and boil at 180° to 185° . It is soluble in 12 parts of water at 15° . **Iso-crotonic acid**, the liquid, is a colorless oily liquid with a strong odor resembling butyric acid. It boils at 172° and melts at about 15° . It mixes with water in all proportions.



Two pairs of higher acids of this series are known, the members of each pair being related to each other as are crotonic and iso-crotonic acids. The first two are known as **tiglic acid** and **angelic acid** and they have been proven to be the *alpha-methyl* substitution products of the two crotonic acids. Tiglic acid is **α -methyl crotonic acid** and is therefore the *cis* form. Angelic acid is **α -methyl iso-crotonic acid** and is the *trans* form.

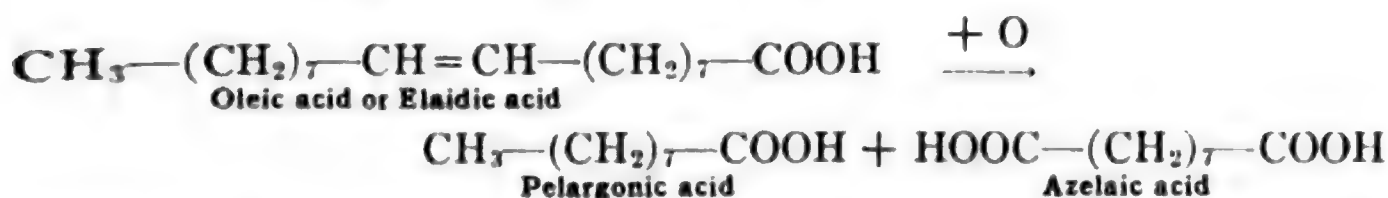


The second pair of higher unsaturated acids exhibiting geometric isomerism is **oleic acid** and **elaidic acid**. Oleic acid is of especial importance because, as a glycerol ester, it occurs very commonly as a constituent of many animal and vegetable *fats* and *oils*. While most

of the acids which occur as esters in fats and oils are members of the saturated series a few unsaturated acids are also found. Oleic acid the most important one belongs to the *ethene series* and is the *eighteen carbon* member, i.e. $C_{17}H_{33}-COOH$, derived from the hydrocarbon $C_{18}H_{36}$. Elaidic acid has the same composition and has been shown to be the *geometric isomer* of oleic acid.

One Double Bond.—That oleic acid and elaidic acid are normal or straight chain compounds each containing *one* double bond is proven by the addition products which they form with hydrogen, in the presence of nickel catalyser, with bromine, hydrobromic acid and water. With these reagents they each yield **stearic acid**, **di-brom stearic acid**, **mono-brom stearic acid** and **mono-hydroxy stearic acid** respectively, adding in each case *two* hydrogen atoms or the equivalent. Also mild oxidation converts them each into **di-hydroxy stearic acid**. As stearic acid has been proven to be the *normal eighteen carbon saturated mono-basic acid*, these reactions prove that oleic acid and elaidic acid both have the structure of a *normal eighteen carbon unsaturated acid* containing *one* double bond.

Position of Double Bond.—The position of the double bond and the full constitution of oleic acid and elaidic acid has been established by means of the products obtained by careful oxidation. It has been shown that when compounds containing a double bond are thus oxidized the effect is to split the compound at the double bond with the oxidation of each doubly linked carbon group to carboxyl. Now both oleic acid and elaidic acid on oxidation yield two acids, each containing *nine* carbon atoms. One is a *mono-basic acid* known as **pelargonic acid**, $C_8H_{17}-COOH$; and the other is a *di-basic acid*, **azelaic acid**, $HOOC-C_7H_{14}-COOH$. The reaction is



This proves that in both of these acids the double bond is between carbon atoms *nine and ten* or in the middle of the straight chain of eighteen carbon atoms.

Conversion of Oleic into Elaidic Acid.—Furthermore, oleic acid, a liquid is easily converted, by means of a small amount of nitrous acid into white solid elaidic acid. This reaction is of the nature of other

reactions by which geometric isomers are transformed into each other. All of these facts go to prove that **oleic acid** and **elaidic acid** are *geometric isomers* exactly analogous to **crotonic acid** and **iso-crotonic acid**. The two acids may thus be represented by the following formulas though it has not been fully established as to which one has the *cis* and which the *trans* form.



Iso-oleic Acid.—It should also be mentioned that a third isomeric ethene unsaturated acid of this composition is known, viz., **iso-oleic acid**. The isomerism in this case is probably *structural* and consists in a change in the *position of the double bond*, which is considered to be between carbon atoms *two* and *three*, viz., $\text{CH}_3-(\text{CH}_2)_{14}-\text{CH}=\text{CH}-\text{COOH}$. Oleic acid was discovered by **Chevreul** in 1846. It is a clear colorless oily liquid without odor or taste and is easily oxidized in the air. On cooling it solidifies to a white crystalline mass melting at 14° . Under a pressure of 10 m.m. it boils at 223° but distills without decomposition at 250° with superheated steam. It differs from the higher saturated acids in yielding a lead salt which is easily soluble in ether, thus affording a method for its separation and isolation. Elaidic acid is a solid melting at about 45° .

As was stated, oleic acid occurs as an ester in many common fats and oils. In common with other unsaturated acids it possesses the characteristic property of forming addition products with the halogens or halogen acids. This property it imparts to the fats and oils in which it is present as an ester giving another important method for the analysis of these substances. This and the other properties and reactions of oleic acid which are important in connection with the analysis of fats and oils will be considered again when we study these substances.

Hypogaecic Acid $\text{C}_{16}\text{H}_{29}-\text{COOH}$

The acid next lower than oleic acid should be mentioned. This is **hypogaecic acid**, the ethene unsaturated acid containing sixteen carbon atoms, $\text{C}_{16}\text{H}_{29}-\text{COOH}$. Together with **arachidic acid** which is the twenty carbon saturated acid, $\text{C}_{19}\text{H}_{39}-\text{COOH}$ it is present as an ester in *peanut oil*. The two acids receive their names from the

botanical name for the peanut plant, *Arachis hypogaea*. They were both discovered by Goessmann in 1854-1855.

Linoleic and Linolenic Acids

We have referred to the fact (p. 162), that compounds of greater unsaturation than the ethine series are known in which the greater unsaturation is due to the presence in the molecule of more than one double or triple bond. From fats and oils three acids have been isolated which are of this character. They are **linoleic acid**, $C_{17}H_{31}-COOH$ derived from the hydrocarbon $C_{18}H_{34}$ or C_nH_{2n-2} and **linolenic acid** and **iso-linolenic acid** both of which have the composition $C_{17}H_{29}-COOH$ derived from the hydrocarbon $C_{18}H_{32}$ or C_nH_{2n-4} . The first of these acids linoleic acid has been shown to contain *two double bonds*, while the last two linolenic acid and isolinolenic acid each contain *three double bonds*. The isomerism of the last two being due to the different positions which the three double bonds occupy. All of these acids possess in a marked degree the properties of unsaturation which properties they confer upon the fats and oils in which they occur as esters. They are all found especially in certain oils, *e.g.*, *linseed oil* possessing properties characterizing them as *drying oils*, due to their easy oxidation. These properties and facts in connection with them will be discussed under fats and oils.

Propiolic Acid $CH \equiv C-COOH$ Propinoic Acid

By the oxidation of propargyl alcohol, propinol, $CH \equiv C-CH_2OH$ (p. 167), an acid is obtained having the constitution $CH \equiv C-COOH$ and known as **propiolic acid** or **propinoic acid** and also as **acetylene carboxylic acid**. This is the simplest acid of the *ethine* series and the only one we shall mention. Derivatives of it are of importance in the **benzene** series in Part II as will be shown later.

C. POLY-SUBSTITUTION PRODUCTS

VI. POLY-HALIDES, -CYANIDES AND -AMINES

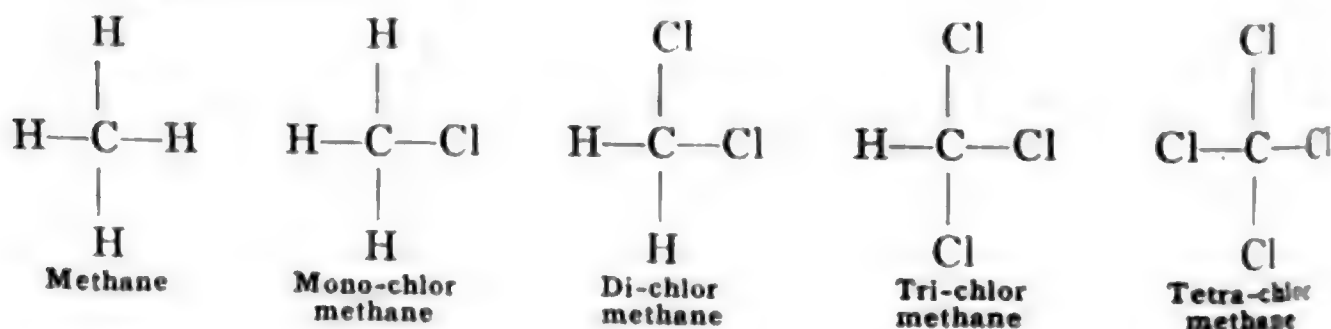
The compounds which we have considered thus far are the hydrocarbons, both saturated and unsaturated and the mono-substitution products derived from them. We have now to consider the compounds which result from the substitution into the hydrocarbon chain of *more than one* element or group. These are known as *poly-substitution products* from the Greek word *poly* meaning many. These compounds are of two kinds; first, those in which the substituting elements or groups are the *same*, termed *poly compounds*; and second, those in which the substituting elements or groups are of *different* character, termed *mixed compounds*. These last may be, for example, mixed halides and alcohols, mixed alcohols and acids, mixed amines and acids, etc. The poly compounds of the first class will include the following groups:

- Poly-halides
- Poly-amines
- Poly-cyanides and iso-cyanides
- Poly-hydroxy compounds or poly-acid alcohols
- Poly-aldehydes
- Poly-carboxy acids or poly-basic acids

A. POLY-HALIDES

I. POLY-HALOGEN METHANES

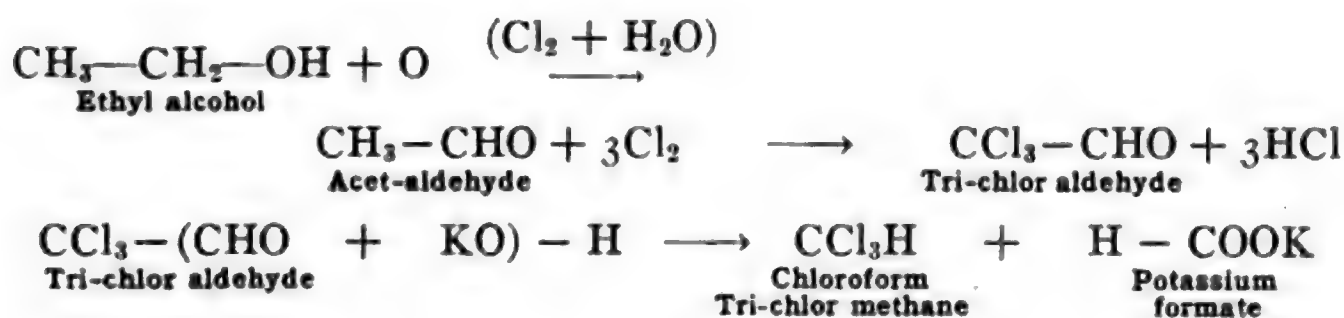
At the very beginning of our study we stated that when methane gas is acted upon by chlorine in the sunlight a mixture of four products is obtained resulting from the substitution of one, two, three or four chlorine atoms for an equivalent number of hydrogen atoms in the methane molecules. These four compounds are represented by the following formulas:



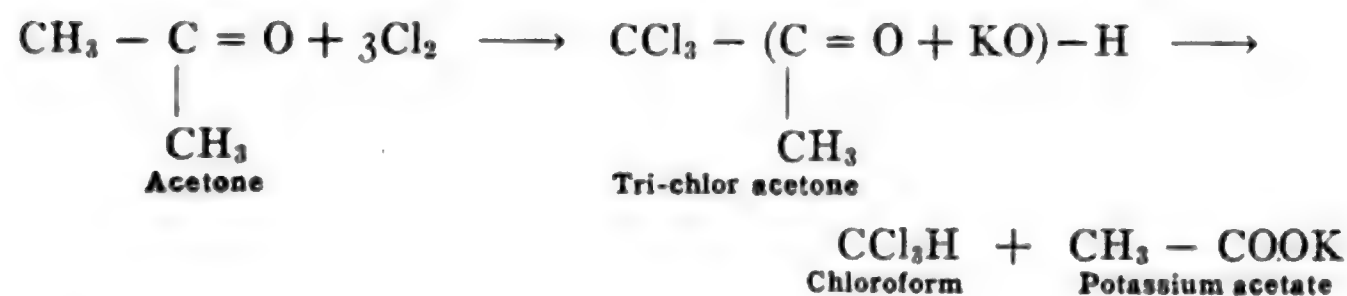
The three poly-chlorine substitution products of methane, as represented above, are all known, but only two of them are of sufficient importance to be considered in detail.

Chloroform CHCl_3 Tri-chlor Methane

The tri-chlorine substitution product of methane is the common and very important *anesthetic chloroform*. It may be made by the method referred to, viz., by the direct chlorination of methane. This method is not, however, a practical one. The industrial preparation is from **alcohol** or **acetone**, by treatment with **chlorine** and an alkali. In the reaction with alcohol the chlorine acts, first, as an oxidizing agent, oxidizing the alcohol to aldehyde. The chlorine then acts as a substituting agent forming a tri-chlorine substitution product of the aldehyde. This tri-chlor aldehyde is then decomposed by the alkali and chloroform results. The steps in this reaction have been definitely proven, as follows:



In practice, the chlorination is effected, not by the use of free chlorine, as such, but by the use of *bleaching powder*, **calcium hypochlorite**. The preparation from acetone is by a similar chlorination. In the reaction which takes place, one of the methyl groups is substituted just as in the case of aldehyde, and then a similar decomposition by means of the alkali takes place.



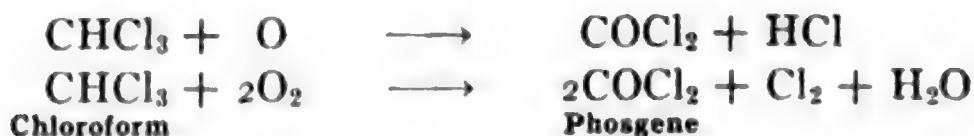
The removal of the carbonyl group by alkalies, producing formic acid, in one case, and the methyl homologue, acetic acid, in the other, is

analogous to the preparation of formic acid from carbon monoxide and potassium hydroxide.



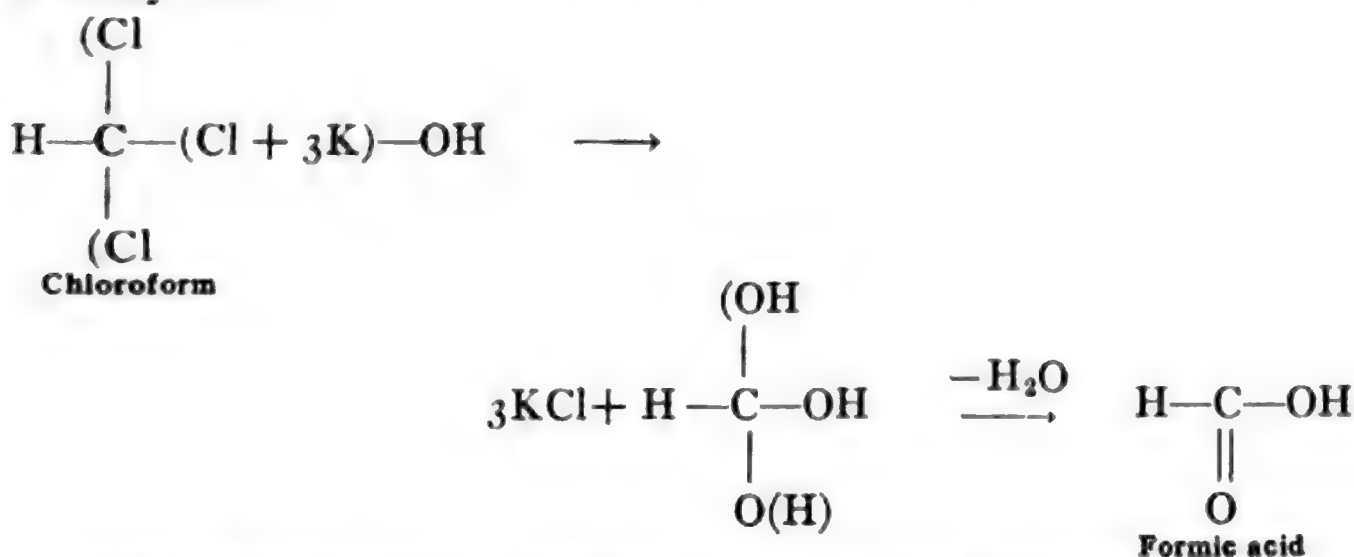
Potassium formate

In the industrial application of this reaction in the preparation of chloroform, a mixture of bleaching powder and dilute alcohol (85-90 per cent.) or acetone, is heated with steam, until action begins. The steam is then cut off as the reaction usually continues without additional heat, oftentimes becoming too violent. When the reaction quiets down steam is again admitted and distillation is begun. The distillate which passes over consists of two layers, a lower heavier layer of chloroform and an upper lighter layer of dilute alcohol or acetone. The chloroform is separated from the lighter liquids and is washed with acid (sulphuric) and then with water. It is then dried with calcium chloride and redistilled as pure chloroform. Chloroform is a heavy, colorless, mobile liquid with a sweet suffocating odor. It melts at -70° and boils at 61° . It has a specific gravity, at 15° , of 1.49. It is only slightly soluble in water and does not mix with it. It is non-inflammable, but imparts a green color to a colorless flame, due to the chlorine present. It was discovered in 1831 by **Liebig and Soubeiran**. Its action and use as an anesthetic was discovered in 1848 by an Englishman, **Simpson**. As an anesthetic it is used, not in a pure state, but with about 1 per cent. of alcohol mixed with it. With this amount of alcohol present the decomposition of the chloroform, by air and light, into chlorine, hydrochloric acid, and **phosgene gas** (COCl_2), is hindered. This decomposition shows the ease with which the chlorine is removed from the compound.

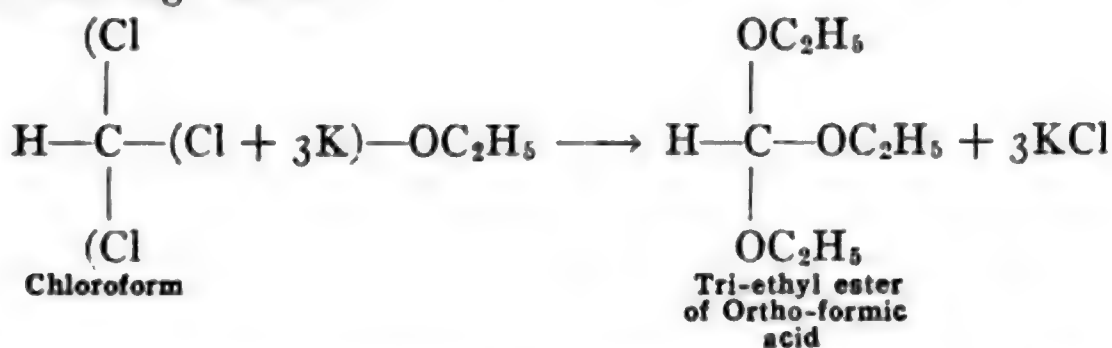


Chloroform Reactions.—This ready giving up of its chlorine is also shown by the reactions of chloroform with alkalies, with ammonia and with amines. With alkalies chloroform yields salts of formic acid. This reaction consists in a replacement of all of the chlorine by hydroxyl yielding a tri-hydroxy methane. As we have previously discussed,

when more than one hydroxyl group is linked to one carbon atom water is always lost.



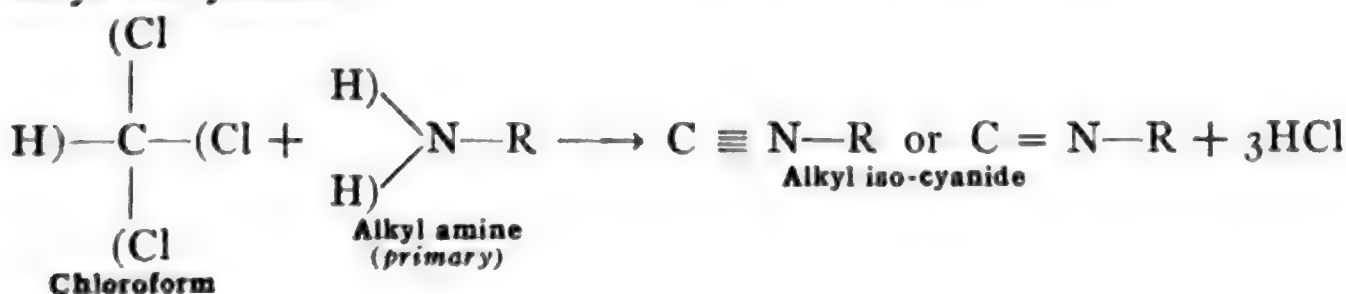
Ortho Formic Acid.—Though the tri-hydroxy methane is not known we have proof that it is formed as the intermediate product in the foregoing reaction, because if we use, instead of potassium hydroxide, the analogous ethoxy compound, viz., **potassium ethylate**, $\text{C}_2\text{H}_5-\text{OK}$, there is obtained as the first result of the reaction the *tri-ethyl ester* of **tri-hydroxy methane**, or as it is known, **ortho-formic acid**, according to the following reaction:



With ammonia, in the presence of alkalies, chloroform yields **hydrogen cyanide**, as follows:



Hofmann's Isonitrile Reaction.—If, however, instead of ammonia we use *alkyl primary amines*, we obtain not the *alkyl cyanides* but the *alkyl iso-cyanides*



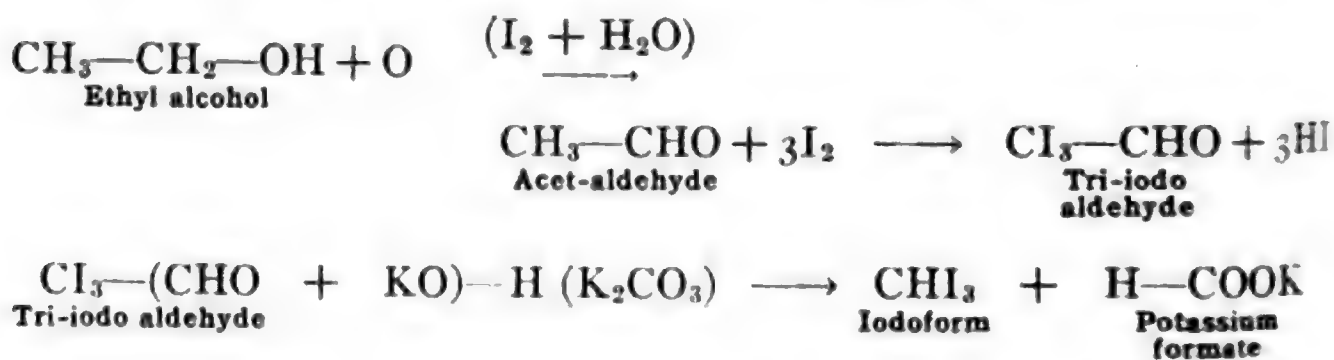
In this reaction the nitrogen changes from tri-valent to penta-valent, or according to the other view in regard to the constitution of iso-cyanides (p. 71), the carbon changes from tetravalent to bivalent. It will be recalled that this reaction has been met with before (p. 70) and is known, as **Hofmann's iso-nitrile reaction**. It is a test for primary amines as it is necessary for the amine to have two hydrogen atoms in order to withdraw two chlorine atoms from the chloroform. The characteristic odor of the iso-nitrile makes the reaction a distinctive test, for either a primary amine or for chloroform.

Bromoform CHBr_3 Tri-brom Methane

This corresponding bromine compound is made by exactly analogous reactions to the ones described above for the preparation of chloroform. The compound is a liquid possessing anesthetic properties though only slightly.

Iodoform CHI_3 Tri-iodo Methane

The corresponding iodine compound is the common substance, **iodoform**. It possesses both anesthetic and antiseptic properties and is a most important surgical disinfectant in the case of wounds or cuts. It is solid, crystallizing in beautiful yellow crystals. It is practically insoluble in water but is soluble in alcohol and ether. It is prepared by reactions exactly analogous to those used in the case of chloroform.



Iodoform Test for Alcohol.—It is made, in practice, by adding iodine to an alkaline (KOH or K_2CO_3), alcohol and water solution. The compound has a characteristic, very penetrating odor which may be detected even though an exceedingly small amount is present. On this account the reaction above may be used as a test for alcohol by simply adding a crystal of iodine and a little alkali to a solution con-

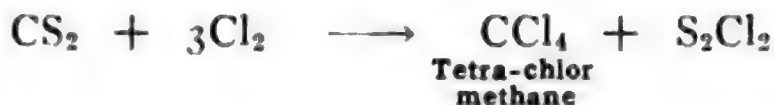
taining alcohol and then warming. By this test as little as 1 part alcohol in 2000 parts water may be detected.

Fluoroform CHF_3 Tri-fluor Methane

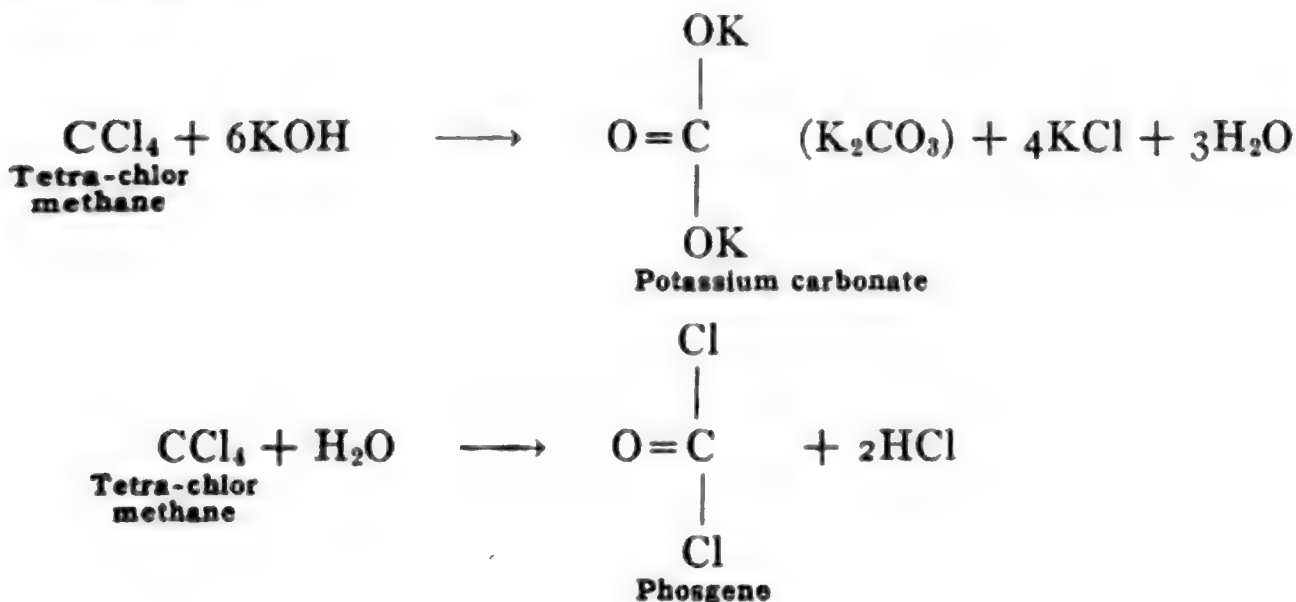
The corresponding fluorine compound is also known, and is a gas with a chloroform-like odor.

Carbon Tetrachloride CCl_4 Tetra-chlor Methane

This is the only tetra-halogen substitution product of methane which will be mentioned. It is produced when methane is chlorinated to its limit. It may also be made by further chlorination of chloroform. The reaction by which it is made industrially is, however, entirely different. It consists in chlorinating **carbon di-sulphide** in the presence of a *carrier* such as iodine. In this reaction, which probably takes place in several steps, the two sulphur atoms, in the carbon di-sulphide, are replaced by four chlorine atoms.



It is a colorless liquid resembling chloroform in odor. It is a good solvent of fats and is much used for this purpose. It is *not inflammable* and is a non-supporter of combustion, acting as a suffocating blanket. This property makes it useful as a non-inflammable fat solvent or cleaning liquid, and also as a fire extinguisher liquid. It undergoes reaction with alkalies similar to that of chloroform, and yields alkali carbonates. With water, at high temperatures, it yields **phosgene**, COCl_2 **carbonyl chloride**.



II. POLY-HALOGEN ETHANES

Di-chlor Ethanes

Isomerism.—When we come to the di-substitution products of ethane we find two classes of isomeric compounds as was discussed briefly on page 53. The fact that in each class only one mono-substitution product of ethane is known has been given as proof that all of the hydrogen atoms in ethane are alike, *i.e.*, ethane, like methane, is a symmetrical compound. When, however, *two* substituting elements or groups are introduced into ethane, *two* isomeric compounds result each having the composition $C_2H_4Cl_2$, in the case of the chlorine product,



Unsymmetrical Di-chlor Ethane.—These two compounds may also be prepared by other reactions which show us what their true constitution is. When acet-aldehyde, which we have previously proven has the constitution represented by the formula, CH_3-CHO , is treated with phosphorus penta-chloride one oxygen atom is replaced by two chlorine atoms and the product is one of the two isomeric di-chlor ethanes.

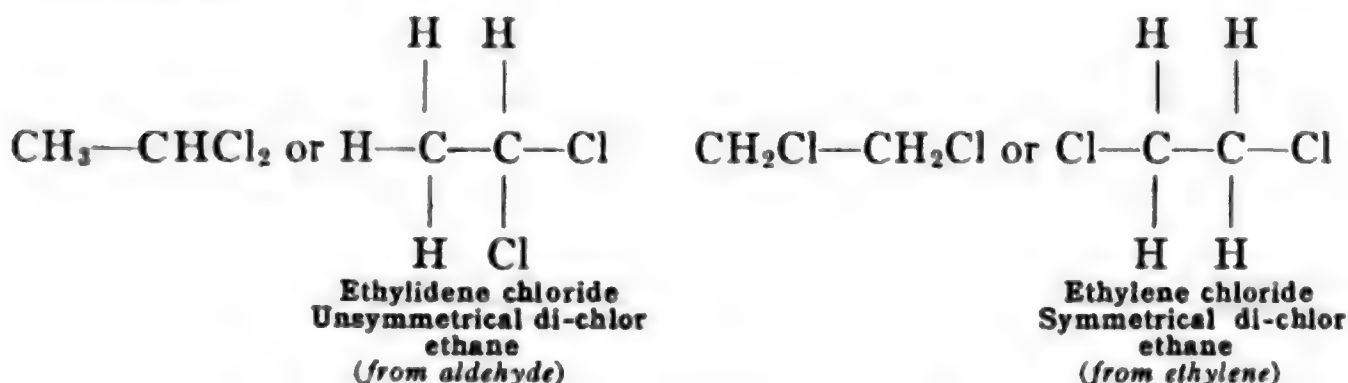


This reaction is entirely different from that of phosphorus penta-chloride on alcohol, in which the hydroxyl of the alcohol is replaced by one chlorine, and the mono-halogen substitution product of the hydrocarbon results (p. 81). If our ideas in regard to the constitution of aldehyde are correct, this reaction must mean, that, in the di-chlor ethane formed in this way, the two chlorine atoms are linked to the *same* carbon atom. Such a structure represents a compound which is plainly *unsymmetrical*.

Symmetrical Di-chlor Ethane.—The isomeric di-chlor ethane is obtained when the unsaturated hydrocarbon **ethylene**, or **ethene** takes up two chlorine atoms, forming an addition product.

According to our ideas in regard to the constitution of the hydrocarbon ethane the only formula for an isomeric di-chlor ethane, differing from the one derived from aldehyde, is one in which the two chlorine atoms instead of being both linked to the *same* carbon atom are each linked to a *different* carbon atom. This gives us a *symmetrical* com-

pound corresponding to the unsymmetrical one just given. The two formulas are:



Ethylene and Ethylidene Compounds.—The fact that the **symmetrical di-chlor ethane** is readily prepared from ethylene, has given to it the name of **ethylene chloride**. To distinguish the two isomers by name the other, the **unsymmetrical di-chlor ethane**, has been called **ethylidene chloride**. In connection with our discussion of the constitution of the ethene series of unsaturated hydrocarbons (p. 154), we have used the constitution of ethylene chloride as proving the constitution of ethylene or ethene, as $\text{H}_2\text{C}=\text{CH}_2$. Isomerism of the character shown in these two di-chlor ethanes, as above explained, is found in all classes of di-substitution products of ethane, so that we may express the compounds by general formulas as follows:



The ethylidene, or unsymmetrical di-halogen substitution products of ethane, are not of much importance, because they do not easily undergo reaction. They are prepared by the reactions just described, viz., from aldehyde by the action of phosphorus penta-chloride, -bromide, or -iodide. Also by the action of phosphorus chlor-bromide, PCl_3Br_2 , or of carbonyl chloride (phosgene), COCl_2 . They may also be made by the further halogenation of the mono-halogen ethanes:



This last reaction is of interest in showing that a second halogen atom, introduced into a compound which already has one substituted halogen, enters the same carbon group in which the first halogen is substituted. The reaction is not, however, all one way, as the symmetrical

compound is also obtained. The proportions of the two compounds depend on the conditions of the reaction and upon the particular reagent used.

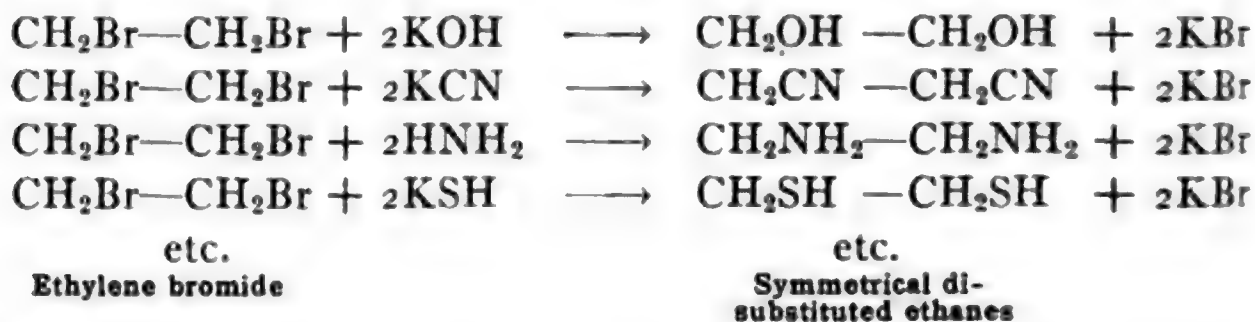
Ethylidene Chloride.— $\text{CH}_3\text{—CHCl}_2$ is a colorless liquid boiling at 57.7° . It does not mix with water and possesses anesthetic properties, though it has no general use as such. It is a by-product in the manufacture of **chloral, tri-chlor aldehyde** (p. 226).

Ethylidene Bromide. $\text{CH}_3\text{—CHBr}_2$, **Ethylidene Iodide**, $\text{CH}_3\text{—CHI}_2$. The former is a liquid boiling at 110.5° , and the latter a liquid boiling at 177° .

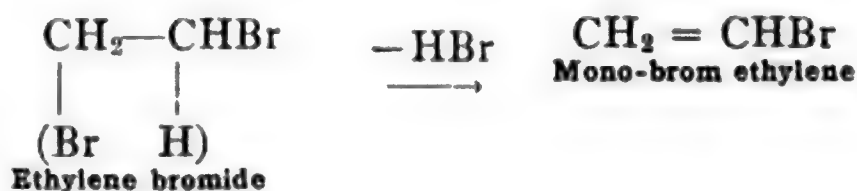
Ethylene Halides $\text{CH}_2\text{X—CH}_2\text{X}$

The ethylene halides may be prepared by direct halogenation of ethane, but this is not a practical method as it yields a mixture of the two isomeric compounds as in the further halogenation of the monohalogen ethanes. The best method of preparation is from the unsaturated hydrocarbon, ethylene. This reaction has been fully considered already (p. 154) and need not be discussed again.

Reactions.—The ethylene halides, especially ethylene bromide, are very important synthetic reagents, as they readily undergo reaction. The halogen is easily replaced by the *hydroxyl group*, *amino group*, *cyanogen group*, etc., yielding the corresponding *symmetrical or ethylene di-substitution products*, as follows:



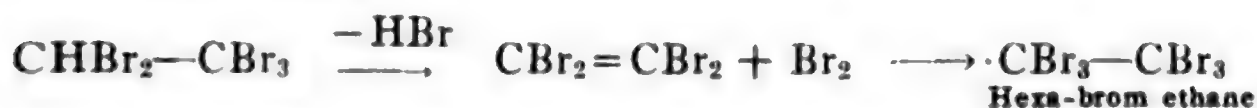
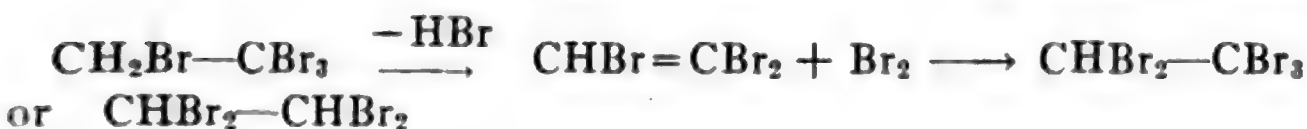
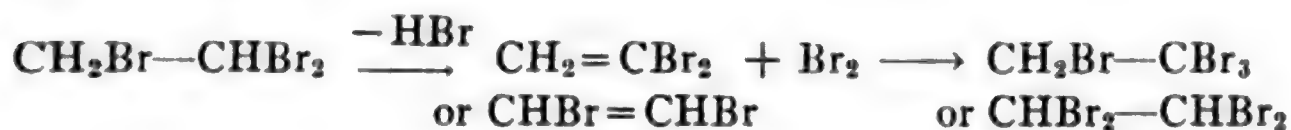
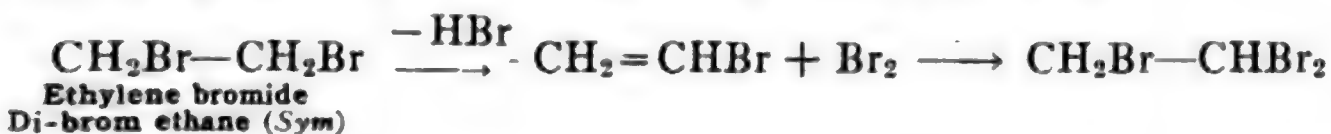
The most important reactions of the ethylene halides are those in a series that takes place with the loss of hydrogen-halide. The hydrogen and the halogen are lost from different carbon groups, with the conversion of the *saturated di-halide* into an *unsaturated mono-halide*, as follows:



The unsaturated compound may then take up two halogen atoms, like the ethylene hydrocarbons themselves, going back again to the *saturated* class of compounds,



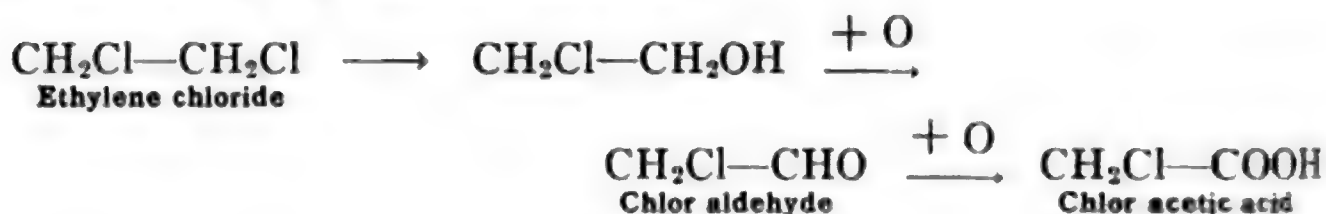
We thus obtain a *tri-halogen* substitution product of the *saturated* hydrocarbon. These reactions may be repeated, yielding, each time, a halogen product of the saturated hydrocarbon containing *one more* halogen atom. We may thus pass from *di-halogen ethane* to *hexa-halogen ethane*. The entire series of reactions is as follows:



One more reaction of the ethylene halides must be mentioned, as, in it, we have a direct proof that the structure of ethane is as represented, viz., the symmetrical structure. Our evidence of this structure, thus far is simply indirect, *i.e.*, from the proof that the other isomeric di-halogen ethane has the unsymmetrical structure.

When ethylene bromide is oxidized **brom-acetic acid** is obtained, *i.e.*, acetic acid in which bromine is substituted in the methyl radical, $\text{CH}_2\text{Br}-\text{COOH}$. Such a compound can result only from a di-brom ethane in which the two bromine atoms were originally linked to different carbon atoms, viz., $\text{CH}_2\text{Br}-\text{CH}_2\text{Br}$. By oxidation one of the carbon groups, containing one bromine atom is converted into carboxyl, and the other, still containing one bromine atom and one only, remains. The same compound is also obtained with intermediate products, when one of the halogen atoms is first replaced by hydroxyl and then subjected to oxidation. The replacement of one halogen by hydroxyl would yield a compound containing primary alcohol group ($-\text{CH}_2\text{OH}$) which on oxidation would be converted first into the aldehyde group ($-\text{CHO}$)

and this by further oxidation, into the acid group (—COOH) as follows, in the case of the chlorine compound:



Higher Halogen Ethanes

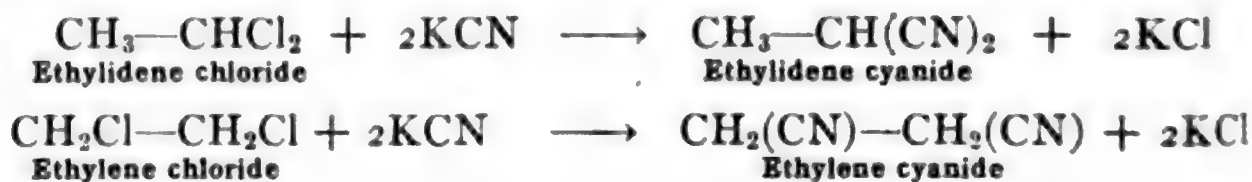
Of the higher halogen derivatives of ethane, representatives of the *tri-, tetra-, penta-* and *hexa-derivatives* are known. Of the tri- and penta-halogen ethanes only one class is known, viz., the unsymmetrical, i.e., $\text{CH}_3\text{—CX}_3$ or $\text{CH}_2\text{X—CHX}_2$, and $\text{CHX}_2\text{—CX}_3$. Of the tetra-halogen ethanes the symmetrical and the unsymmetrical are both known, exactly analogous to ethylene chloride and ethylidene chloride:



The hexa-halogen ethanes, $\text{CX}_3\text{—CX}_3$, or per-halogen ethanes, are known in both the chlorine and the bromine compounds. **Per-chlor ethane**, $\text{CCl}_3\text{—CCl}_3$, **hexa-chlor ethane** is a colorless, crystalline substance with a camphor-like odor and which melts at 184° . **Per-brom ethane**, $\text{CBr}_3\text{—CBr}_3$, **hexa-brom ethane** is also a colorless, crystalline substance.

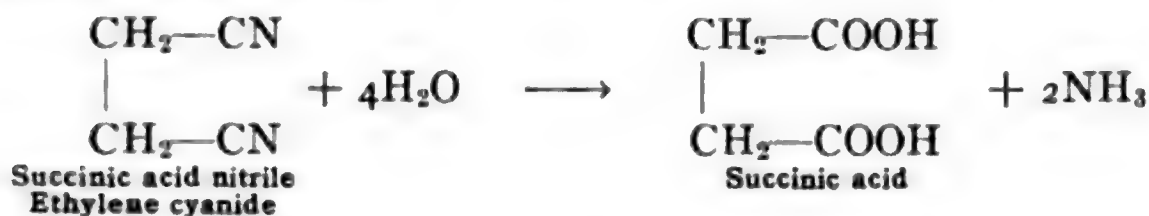
B. POLY-CYANIDES

The next group of poly-substitution products are those containing two or more *cyanogen radicals*, (—CN). These correspond exactly to the poly-halogen compounds, from which they may be prepared by the action of potassium cyanide.



These compounds are characterized by the same properties as the mono-cyanogen compounds. As the latter are known as acid nitriles, because on hydrolysis they yield mono-carboxy acids, so also the di-cyanogen compounds are *nitriles of the di-carboxy acids*. The symmetri-

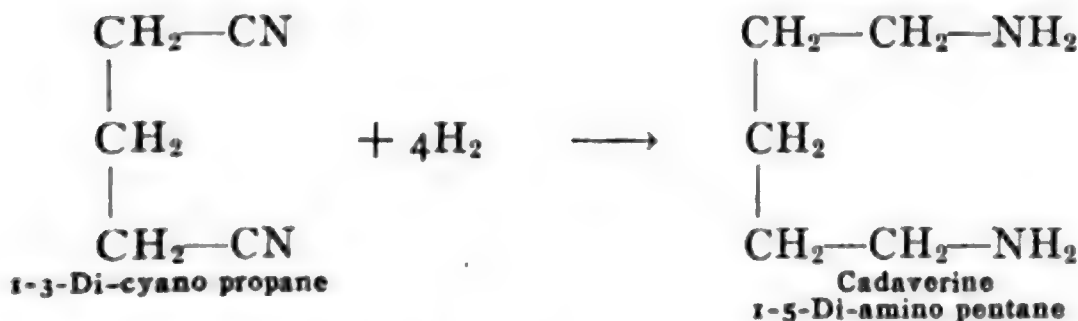
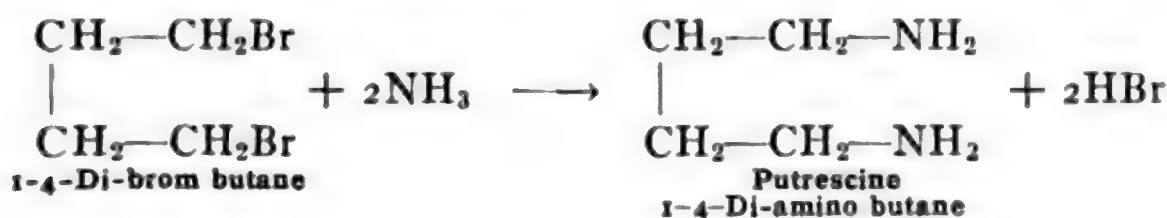
cal di-cyanogen ethane or ethylene cyanide yields a di-carboxy acid known as succinic acid



These di-cyanogen and other poly-cyanogen derivatives are of importance only in this connection as *nitriles of the poly-carboxy acids* and those that are necessary to be considered will be referred to later as we come to them in the study of these acids. The simplest di-cyanogen compound is the gas **cyanogen** NC—CN, which has been referred to as an example of a radical which exists as such in the free state.

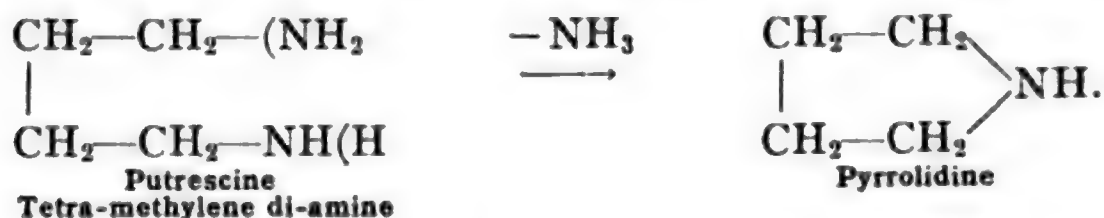
C. POLY-AMINES

Putrescine and Cadaverine.—The *poly-amines* may be obtained by the reduction of *poly-nitro compounds* or *poly-cyanogen compounds* (pp. 70, 75). In the former case the amine has the *same number* of carbons as the nitro compound but in the latter case the amine has *two more* carbons than the radical of the di-cyanogen compound. The usual method of formation, however, is the one already used in preparing the mono-amines, viz., from the corresponding halogen compound by action of ammonia.

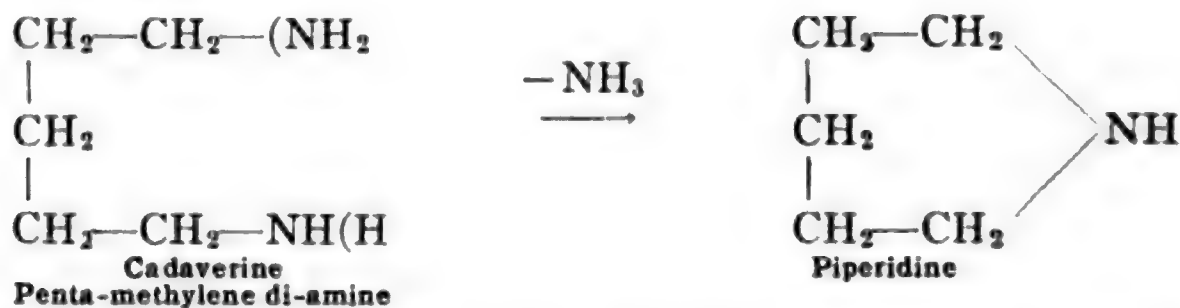


The di-amines are *strong di-acid bases* with ammoniacal odor and readily form salts with acids. The di-amines of the higher hydrocarbons, in which the two amine groups are attached to the end carbon atoms, are known as *poly-methylene compounds* because all of

the carbon hydrogen groups are ($-\text{CH}_2-$). They exhibit an interesting property of losing ammonia and yielding an *anhydride-like compound*. The reaction takes place with the hydrochloric acid salts.



Imines.—The compounds so formed and containing the group ($-\text{NH}-$), are known as *imines*. The four carbon imine given above is named **pyrrolidine**, and the di-amine from which it is formed, as **tetra-methylene di-amine**, also as **putrescine**. It is found as a putrefaction product of animal flesh. The analogous five carbon compounds are, **penta-methylene di-amine**, or, **cadaverine**, and the imine is **piperidine**. The last compound is found in **pepper** in combination as the alkaloid, **piperine**.



Hetero-cyclic Compounds.—In the formation of these imines the *open chain* structure of the di-amine compound is converted into a *closed chain*, or *ring* structure of the imine. As the ring thus formed contains not only carbon groups but also a nitrogen group the compounds are termed *hetero-cyclic*. These compounds are of importance, and will be used later, in showing the connection between the two great classes of organic compounds, viz., the *open chain*, or *acyclic* compounds, such as the saturated and unsaturated compounds which we have been studying, and the *closed chain*, or *cyclic* compounds, which we shall study later, in connection with **benzene** and its derivatives.

VII. POLY-HYDROXY COMPOUNDS—POLY-APCOHOLS

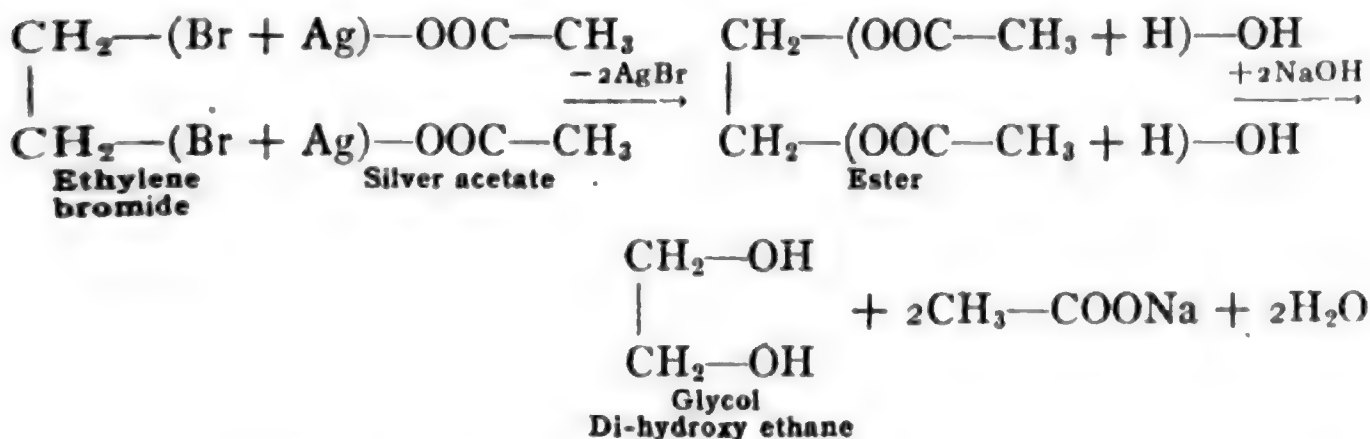
A. DI-HYDROXY ALCOHOLS—GLYCOLS

Glycol $\text{HO—H}_2\text{C—CH}_2\text{—OH}$ Ethylene Glycol

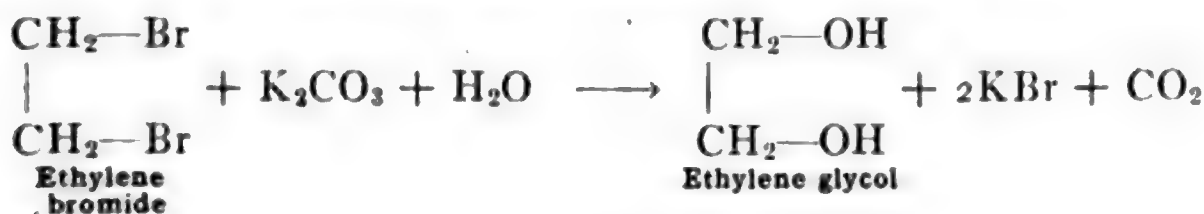
When alkyl mono-halides are treated with silver hydroxide, AgOH , or with potassium hydroxide, KOH , the halogen is replaced by the hydroxyl group and mono-hydroxy alcohols result.



In a similar way, when ethylene bromide is treated with silver acetate, $\text{CH}_3\text{—COOAg}$, an acyl-ester of the corresponding di-hydroxy alcohol is obtained, which, on hydrolysis, yields the *di-hydroxy alcohol* itself, as follows:



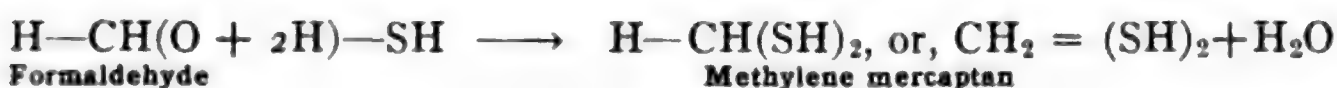
Glycol.—This synthesis of di-hydroxy ethane was discovered by **Wurtz**, in 1854. The compound was named by him, **glycol**, because of its sweet taste. It is known also as **ethylene glycol**. The synthesis may be modified by substituting potassium acetate for the silver salt. Also, ethylene bromide is converted directly into the di-hydroxy compound, by boiling with dilute potassium carbonate.



DI-VALENT MERCAPTANS, THIO-GLYCOLS

The sulphur analogues of the glycols, *i.e.*, **thio-glycols**, or **di-valent mercaptans** are definitely known compounds. Furthermore, it is found, that when sulphur replaces oxygen, in compounds of this class, *two sulph-hydrogen groups* ($-\text{SH}$), *may be linked to one carbon atom and a stable compound result.*

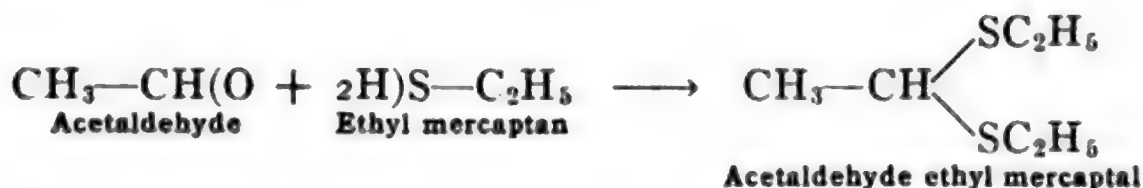
Methylene mercaptan, $\text{CH}_2 = (\text{SH})_2$, is a well known compound and may be made from formaldehyde by treatment with hydrogen sulphide:



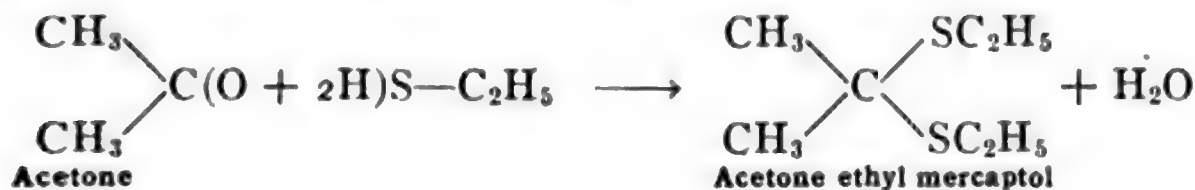
Similarly **ethylidene mercaptan** may be obtained from acetaldehyde:



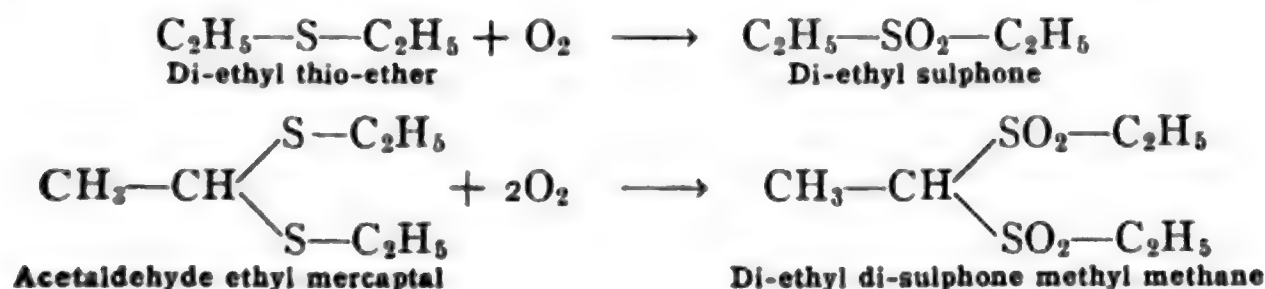
Mercaptals and Mercaptols.—Ethylidene mercaptan is ordinarily obtained as the *thio-ether* by the action of **ethyl mercaptan** on acetaldehyde:

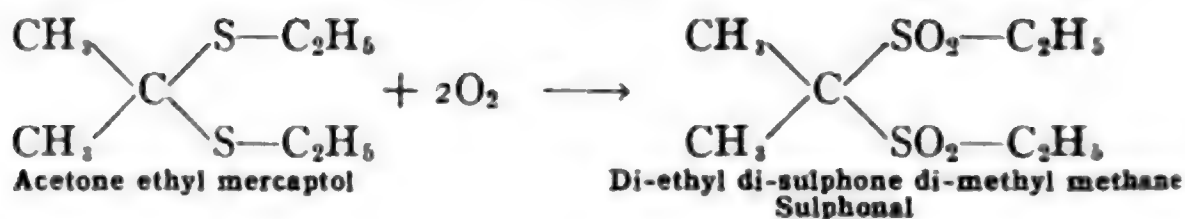


Such a di-thio-ether is known as a **mercaptal** and this particular one is known as **di-thio acetal** (p. 117). Analogous compounds obtained from ketones, *e.g.*, from acetone, are called **mercaptols**.



Like the mono-thio-ethers, these di-thio-ethers yield sulphones, *i.e.*, **di-sulphones**, on oxidation.



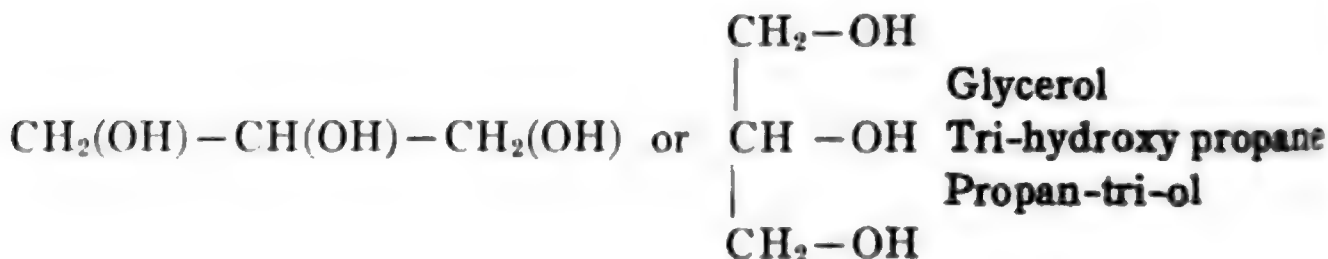


Sulphonal.—This last compound is known as **sulphonal**, and is an important medicinal substance possessing soporific properties. It is a solid forming colorless crystals which melt at 125° – 126° . It is soluble in alcohol and in hot water, slightly in cold.

B. TRI-HYDROXY ALCOHOLS



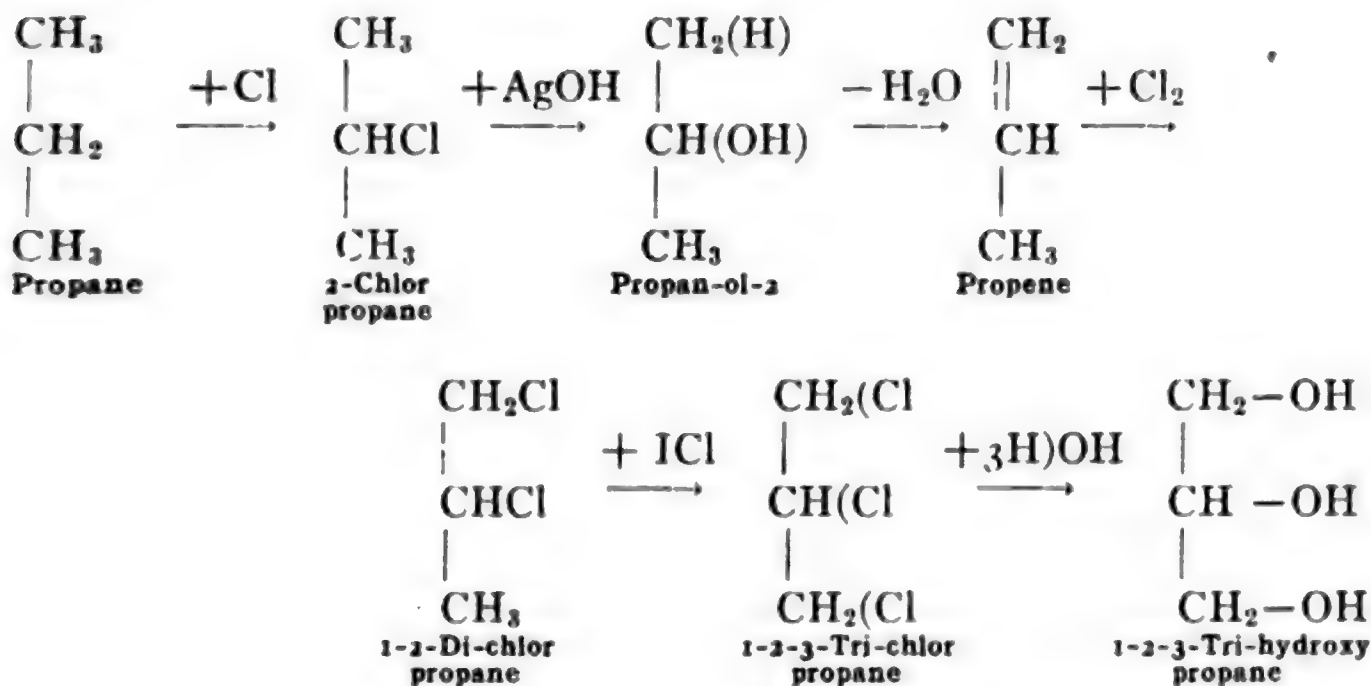
As more than one hydroxyl group linked to a single carbon atom results in an unstable compound, the simplest di-hydroxy alcohol is the one derived from the two carbon hydrocarbon ethane (*i.e.*) di-hydroxy ethane, or glycol, $\text{CH}_2-(\text{OH})-\text{CH}_2(\text{OH})$. Similarly the simplest tri-hydroxy alcohol is derived from the three carbon hydrocarbon propane. It is known commonly as **glycerin**, but is better termed **glycerol**, as the termination, *ol*, signifies an *alcohol*.



Synthesis from Propane.—The constitution of glycerol has been established by a series of reactions, as follows: When secondary, or **iso-propyl alcohol**, **propan-ol-2**, is dehydrated an unsaturated compound is formed, viz., propene, the three carbon member of the ethylene series of hydrocarbons. When propene is treated with halogens, *e.g.* chlorine, two atoms of the halogen add on directly and a saturated di-chlor compound results (see p. 158).

This compound, on further chlorination by means of iodine monochloride, ICl , yields **tri-chlor propane**. On heating with water this hydrolyzes and three hydroxyl groups take the place of the three chlorine atoms.

Writing the reactions in one scheme we can follow the relationship very readily.



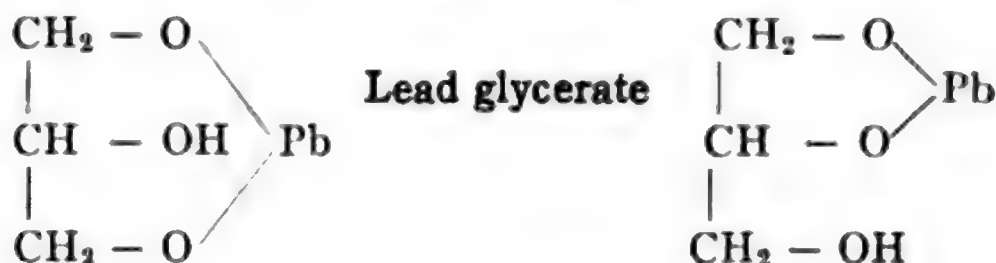
Glycerol must be, therefore, **1-2-3-tri-hydroxy propane**, as represented by the above formula.

Properties.—It is a thick syrup-like liquid more or less oily in its feeling and, on this account, was at one time called an oil. It is not, however, an oil but a true alcohol though as we shall see, it is directly and intimately related to the vegetable and animal fats and oils. It is colorless, odorless and very hygroscopic. It has a sweet taste similar to that of the di-hydroxy compound, glycol, and mixes in all proportions with water and with alcohol, indicating, thus, its alcohol character. It is a stable compound and dissolves many organic, and some inorganic substances. It is non-irritating, softens the skin, when applied to it, and is used as a solvent, or medium, in which many medicinal substances are taken internally. All of these properties give it many important uses both in the industries and in medicine. When cooled for a long time to 0° , it crystallizes, the crystals melting again at 17° . It boils, undecomposed, at 290° , and has a specific gravity of 1.2. In its chemical properties, glycerol acts as an alcohol, forming derivatives characteristic of alcohols. As may be seen, from its constitution, it contains both *primary* and *secondary* alcohol groups. Its derivatives, therefore, are characteristic of both of these classes of alcohols.

DERIVATIVES OF GLYCEROL

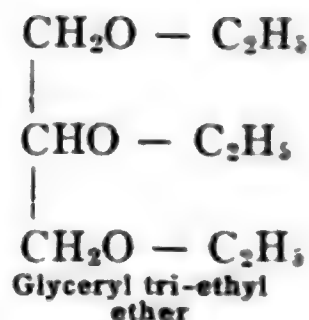
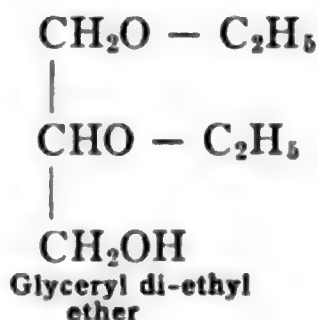
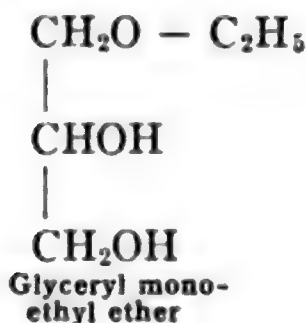
1. SALTS

Analogous to the alkali salts of the alcohols, *e.g.*, $\text{C}_2\text{H}_5\text{—ONa}$, sodium ethylate, glycerol forms salts with several of the metals, in which, one, two or three of the hydroxyl hydrogen atoms are replaced by metals. Both a mono-sodium and a di-sodium glycerate are known. The most important salt of glycerol is, perhaps, the lead salt. Lead being bi-valent, replaces two hydrogens and may form compounds represented by the two following formulas:



2. ETHERS

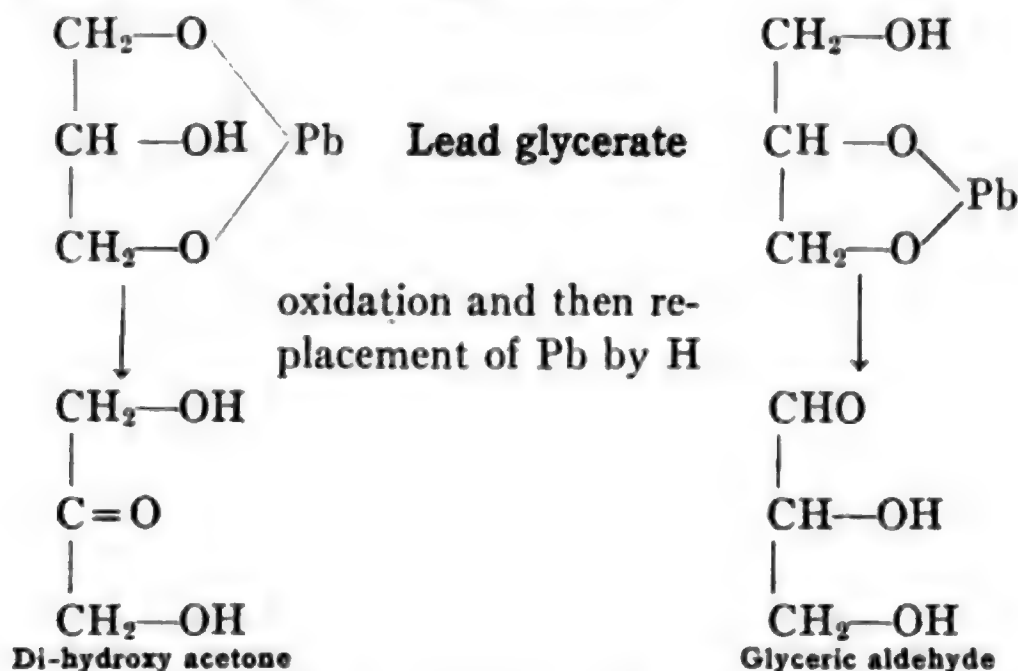
Glycerol also forms ethers with ethyl alcohol and all three of the possible ones are known.



3. OXIDATION PRODUCTS

As glycerol contains *both primary and secondary* alcohol groups, the oxidation products will include *aldehydes, ketones and acids*, and the latter may be either *mono- or di-basic*. On complete oxidation the products are **formic acid** and **carbon dioxide**. The most important of the oxidation products are the two obtained when the lead salt of glycerol is oxidized by means of bromine and the lead then replaced by hydrogen. As the lead, in the lead salt, protects two of the carbon groups and prevents their being oxidized, only one of the original alcoholic groups will be oxidized. As this may be in one case a primary alcohol group and in the other a secondary alcohol group, we may obtain

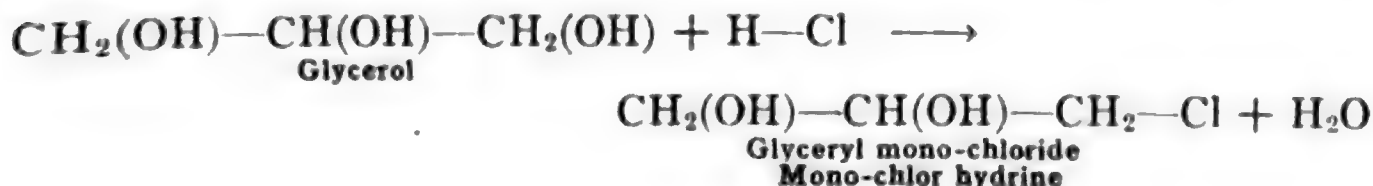
from such oxidation either an aldehyde or a ketone compound. This will be clear from the following reactions:



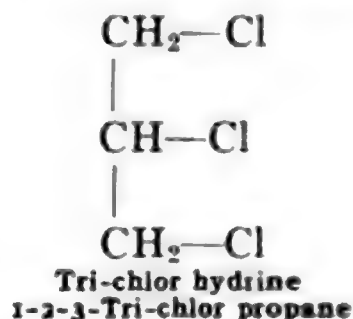
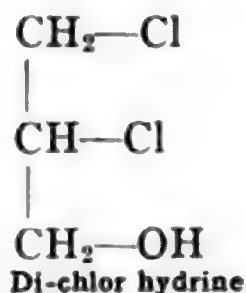
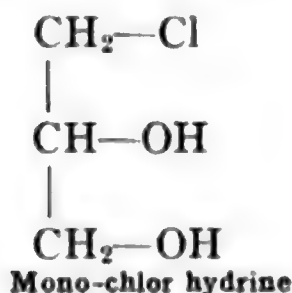
Glycerose.—These two products, the aldehyde and the ketone of glycerol, are of especial importance, as we shall see later, because a mixture of the two known as **glycerose** is the simplest of the large and very important class of compounds known as the **carbohydrates**, of which the **sugars** form a subdivision. On further oxidation of glyceric aldehyde the aldehyde group becomes converted into the carboxyl group and an acid results, known as **glyceric acid**. $\text{CH}_2(\text{OH})\text{—CH}(\text{OH})\text{—COOH}$. In a similar way the other primary alcohol group may be oxidized to carboxyl and a di-basic acid obtained, $\text{HOOC—CH}(\text{OH})\text{—COOH}$, **hydroxy malonic acid**. These will all be considered again later when we discuss the hydroxy acids.

4. INORGANIC ACID ESTERS

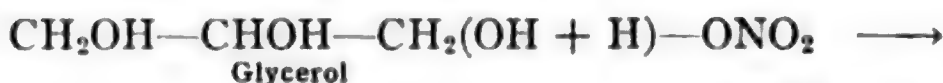
By far the most important group of derivatives of glycerol is that of the *esters* or *ethereal salts*. Just as ethyl alcohol and hydrochloric acid yield an ester, $\text{C}_2\text{H}_5\text{—Cl}$, **ethyl chloride**, so glycerol yields derivatives in which the hydroxyl groups are replaced by halogens. These compounds are formed, both by the action of the hydro-halogen acid, and also, by the action of the phosphorus tri-halogen compounds, *e.g.*, phosphorus tri-chloride, PCl_3



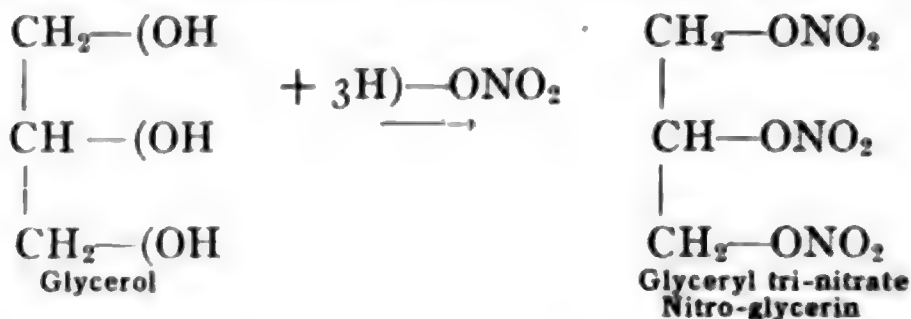
Hydrines.—Such a compound is known as a *halogen hydrine*, or more specifically as a **chlor hydrine**. All three of the chlor hydrines, viz., the mono-, di- and tri-chlor hydrines are known, as follows:



The tri-chlor hydrine is plainly tri-chlor propane, a simple tri-halogen substitution product of propane. It has already been mentioned in connection with the synthesis of glycerol from propane. Of the esters which glycerol yields with the inorganic acids those formed with nitric acid are the most important.



Nitric Acid Esters.—All three of the nitrates are known and when glycerol is completely nitrated it is the *tri-nitrate* which is formed.



Nitro Glycerin.—Glyceryl tri-nitrate is the common and valuable explosive commonly known as **nitro-glycerin**. It is prepared by treating glycerol with a mixture of nitric and sulphuric acids. The nitro-glycerine separates as an oily liquid which is colorless and odorless but has a burning sweet taste. It is insoluble in water but soluble in alcohol and in benzene. It solidifies at 8°. It is poisonous but in small doses is an important medicine, acting as a heart stimulant.

Dynamite.—The most important property of the substance is its great explosive power when detonated. It can, however, be burned glowly without exploding. As an explosive it is not generally used in its pure liquid form but is mixed with an inactive powder material, such

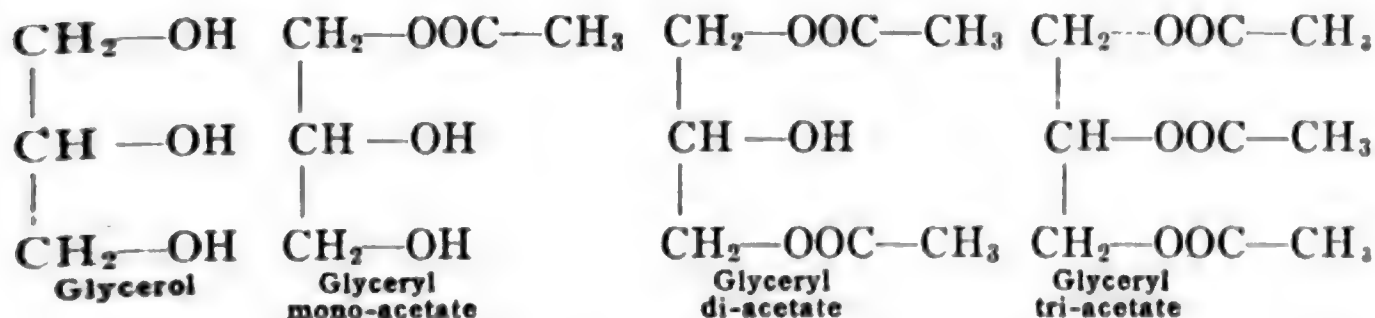
as infusorial earth. In this form, known as **dynamite**, it retains all of its explosive properties and can be handled more easily and safely. If, instead of mixing nitro-glycerine with infusorial earth it is dissolved in **collodion**, which is a nitrated cellulose, to be studied later, a product is obtained known as **gelatin powder**, which possesses like explosive properties and has certain practical advantages.

Nobel.—It is interesting to know, that both of these practical applications of nitro-glycerine, viz., dynamite and gelatin powder were invented by a Swede by the name of **Nobel** who left his money made from the invention of these powerful explosives, for the establishment of prizes in connection with the promotion of peace and known as the **Nobel Peace Prizes**.

5. ORGANIC ACID ESTERS

FATS AND OILS

The esters which glycerol forms with the organic acids of the open chain series or *fatty acids* as they are known, are of especial importance. They are the chief constituents of the widely distributed natural *fats* and *oils* of the animal and vegetable kingdoms. The oils termed *mineral oils*, do not belong to this group, but are *hydrocarbons*, as has already been discussed, (p. 40). Just as glycerol forms mono-, di- and tri-acid esters with the inorganic acids, so with organic acids, it forms esters of the same character. With acetic acid, *e.g.*, we have the three following compounds, which illustrate the esters of glycerol with organic acids.

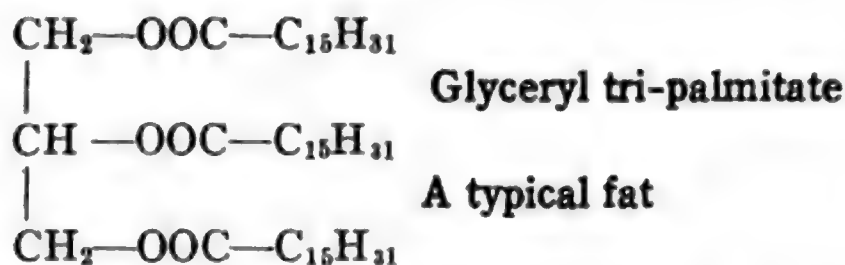


The most important esters of this class are, the *neutral* or *tri-acid esters* of glycerol with the *higher acids* of the *saturated* and the *unsaturated series*. The most important acids, in this connection, are given in the following list:

ACIDS OCCURRING AS ESTERS IN FATS AND OILS

Saturated acids		Unsaturated acids	
Hydrocarbon, C_nH_{2n+2}	Acid, $C_nH_{2n}O_2$	Hydrocarbon, C_nH_{2n}	Acid $(C_nH_{2n-2})O_2$
Butyric acid.....	C_4H_7-COOH	Crotonic and iso-cro- tonic acids.....	C_4H_5-COOH
Caproic acid.....	$C_6H_{11}-COOH$	Hypogaecic acid.....	$C_{15}H_{29}-COOH$
Caprylic acid.....	$C_7H_{13}-COOH$	Oleic and elaidic acids..	$C_{17}H_{33}-COOH$
Capric acid.....	$C_9H_{17}-COOH$	Hydrocarbon, C_nH_{2n-1}	Acid $(C_nH_{2n-4})O_2$
Lauric acid.....	$C_{11}H_{21}-COOH$	Linoleic acid.....	$C_{17}H_{31}-COOH$
Myristic acid.....	$C_{13}H_{25}-COOH$	Hydrocarbon, C_nH_{2n-1}	Acid $(C_nH_{2n-4})O_2$
Palmitic acid.....	$C_{15}H_{31}-COOH$	Linolenic and iso-lin- olenic acids.....	$C_{17}H_{29}-COOH$
Stearic acid.....	$C_{17}H_{33}-COOH$		
Arachidic acid.....	$C_{19}H_{39}-COOH$		

Constitution of Fats and Oils.—These acids which have all been previously discussed (pp. 136 and 170) embrace the more common ones that are found as esters in most oils and fats. The tri-acid ester of glycerol and palmitic acid may be taken as an example of a typical fat. It is exactly analogous to the ester of glycerol and acetic acid which we have just considered, and its formula is:



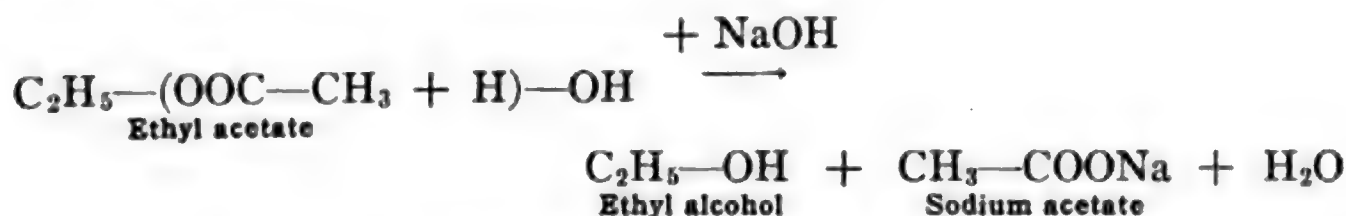
These esters may be prepared synthetically by reactions already referred to in connection with the general methods for the preparation of esters (p. 143). In the case of the palmitic acid esters, the mono-, di- and tri-palmitates have all been prepared by these synthetic methods.

Chevreul. Berthelot.—The most important fact, however, in connection with these esters of glycerol and the higher fatty acids, is, that they are found in such wide and general distribution in nature, in the form of fats and oils. The true chemical nature of animal and vegetable fats and oils was first shown by the French chemist **Chevreul**, in 1815 and later established by **Berthelot** in 1860. They have the constitution of *glycerol esters of the higher saturated and unsaturated acids*. The different fats and oils are distinguished from each other by the *different acid radicals*, and the *different proportions of them*,

which are contained as component parts of the glycerol esters. Fats are *not pure chemical individuals* but are *mixtures* of several in some cases eight or ten, different esters. While the acid radical components differ the alcohol radical component is always the *same*, viz., that of **glycerol**. A single fat may contain several esters but, in a particular fat, both the acid radicals present and the proportions of them, are definite and constant.

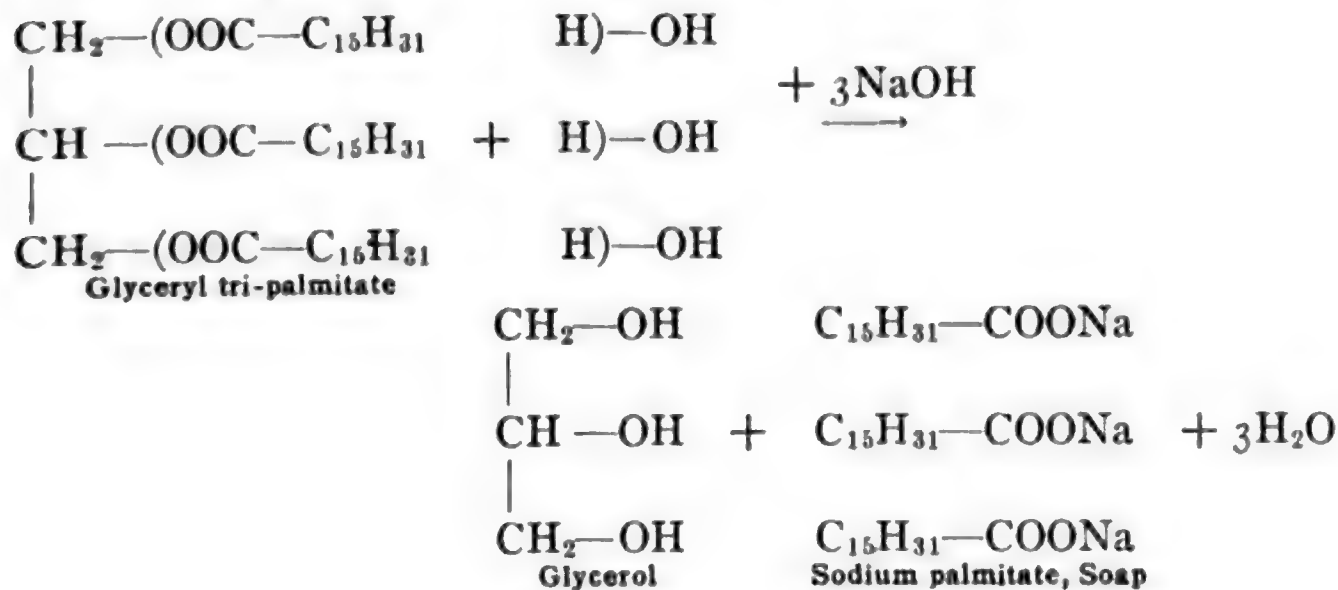
Reactions of Fats and Oils.—The most important reaction of fats and oils is the one by which they are decomposed into their constituent acids and glycerol. By this reaction the particular acid or acids may be determined either qualitatively or quantitatively.

Hydrolysis.—When an ester is boiled with water, or with water and an alkali (p. 141) it is decomposed into the alcohol and acid from which it is derived. The alkali present converts the acid into the corresponding salt so that the final products of the reaction are the alcohol and the salt of the acid.



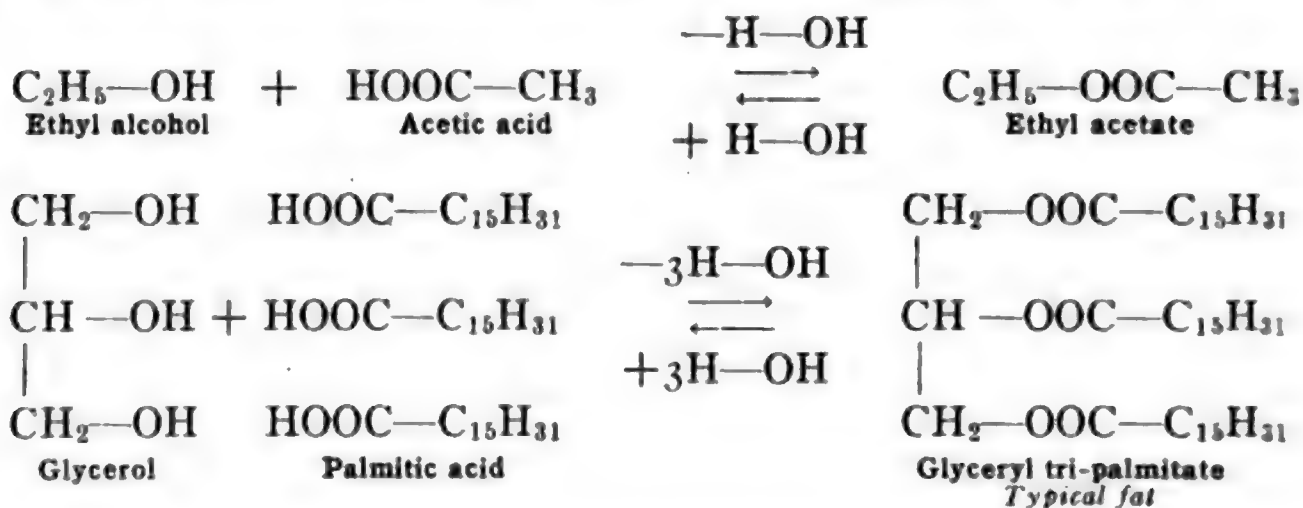
This reaction, it will be recalled, is *typical of all esters*, or ethereal salts. Because it is, in fact, a reaction due to the action of water, it is known as *hydrolysis*. It is the reverse of the reaction of *esterification*.

Saponification.—With a fat, which is a glycerol ester of a higher fatty acid, typified by **glyceryl tri-palmitate**, the reaction yields **glycerol** and the *salt of the acid*, or acids, present, as follows:



The *sodium or potassium salt of palmitic acid, or of stearic acid* or the mixed salts of several acids obtained from ordinary fats, is the common substance known as **soap**. This particular reaction of hydrolysis, is, therefore, known, also, as a reaction of *saponification* (soap formation). Strictly speaking the reaction of saponification applies only to the alkaline hydrolysis of fats, *i.e.*, of glycerol esters, but, as the hydrolysis of other esters is a reaction of exactly the same character, the term is used to apply equally to the hydrolysis of any ester in presence of an alkali. In the case of the lower alcohol and lower acid esters, *e.g.*, ethyl acetate, the salt formed is not a soap but is a crystalline salt, sodium acetate.

As has been previously discussed, the reactions of hydrolysis and esterification constitute a typical reversible reaction. We have, then, the two following examples of this general reversible reaction:



As we shall see, hydrolysis takes place with other compounds than esters usually in the presence of some catalytic agent, such as enzymes, so that the term hydrolysis refers generally to the decomposition of a compound by means of water, while saponification refers to the particular hydrolysis of an ester by means of water in the presence of an alkali, the product being a soap or a crystalline salt.

As commercially made by the saponification of fats, soaps are not pure chemical individuals but consist of a mixture of the alkali-metal salts of the several fatty acids contained as esters in the original fat or oil. The composition of soap, therefore, depends upon the composition of the fat from which it is made. As the common fats and oils which are used for this purpose contain, mostly the glycerol esters of **palmitic, stearic and oleic acids**, the common soaps are mixtures of **sodium, or potassium, palmitate, stearate and oleate**. We shall consider now,

the composition and properties of some of the more common and important fats and oils of animal or vegetable origin.

General Properties of Fats and Oils.—Fats differ from oils simply in their physical properties, the fats being solid at ordinary temperatures while the oils are liquid. They both have exactly the same general character as regards their chemical composition and constitution, as we have above discussed. The acids which are present as glycerol esters are the mono-basic acids of the saturated and the unsaturated series. As we have stated, the fats and oils are complex mixtures of several esters, in some cases as many as eight or ten and their physical and chemical characters will depend, therefore, upon the characters of the different esters present and the proportions in which these occur.

Glycerol Esters.—All of the esters present in fats are **glycerol esters**, and, in most cases, the *neutral* or *tri-acid* ester. The characteristic thing in each ester is therefore the particular acid radical present. The esters of fats have been given names derived from those of the various acids. In place of the termination *ic* of the acid we use the termination *in*. For example, the tri-palmitic acid ester of glycerol, or, **glyceryl tri-palmitate**, is called, **tri-palmitin**, or, simply **palmitin**. Similarly the esters of **stearic**, **oleic** and **butyric acids** are called, **stearin**, **olein**, and **butyrin**. The prefixes, *mono*, *di*, and *tri* are also used to indicate whether the ester has one, two or three acid groups present. The properties of a fat, therefore, which contains a mixture of palmitin, olein, and stearin will correspond to the properties of these individual esters according to the proportions in which they are present. Some of these esters have never been prepared in a pure state, so that we know of their properties only in a general way, as deduced from those of the fats in which they are present.

Table XV gives the more common esters, the fats in which they are most abundant, and the corresponding acids, with the properties of each so far as determined.

Analytical Methods.—For purposes of identification and analysis the distinguishing properties and reactions of fats depend upon the properties of the esters of which they are composed and also upon those of the acids which result on saponification. While it is not the purpose of this study to discuss methods of analysis we shall mention, briefly, the most important properties and reactions of the fats by means of which they may be identified or analyzed. For more detailed information in

TABLE XV.—GLYCEROL ESTERS, FATS

Ester	M.P.	B.P.	Fat or Oil	M.P. or S.P.	Properties
<i>Saturated Series</i>					
Butyrin.....	...	285°	Butter fat	29°, 35°	Non-drying
Caproin.....	Cocoanut oil	20°, 28°	Non-drying
			Butter fat	29°, 35°	Non-drying
Caprylin.....	Cocoanut oil	20°, 28°	Non-drying
			Human fat	Non-drying
			Butter fat	29°, 35°	Non-drying
Caprin.....	Goats-milk fat	Non-drying
			Cocoanut oil	20°, 28°	Non-drying
			Cod-liver oil	liquid	Non-drying
			Butter fat	29°, 35°	Non-drying
Laurin.....	Laurel oil	32°, 36°	Non-drying
			Cocoanut oil	20°, 28°	Non-drying
Myristin.....	53°	Cocoanut oil	20°, 28°	Non-drying
			Butter fat	29°, 35°	Non-drying
			Nutmeg oil	Non-drying
Palmitin.....	62°	Palm oil	27°, 42°	Non-drying
			Lard	28°, 45°	Non-drying
			Butter fat	29°, 35°	Non-drying
			Cocoa butter	30°, 34°	Non-drying
			Human fat	Non-drying
Stearin.....	55°	Tallow	36°, 40°	Non-drying
			Lard	28°, 45°	Non-drying
			Butter fat	29°, 35°	Non-drying
			Human fat	Non-drying
Arachidin.....	Peanut oil	- 5°	Sl.-drying
			Maize oil	- 20°, - 10°	Sl.-drying
			Olive oil	+ 4°, - 6°	Non-drying
<i>Unsaturated Series</i>					
Hypogæin.....	Peanut oil	- 5°	Sl.-drying
Olein.....	liquid	Olive oil	+ 4°, - 6°	Non-drying
			Cotton-seed oil	+ 1°, - 10°	Sl.-drying
			Lard	28°, 45°	Non-drying
			Butter fat	29°, 35°	Non-drying
			Human fat	Non-drying
Linolein.....	liquid	Linseed oil	- 20°, - 27°	Drying
			Poppy oil	- 18°	Drying
			Peanut oil	- 5°	Sl.-drying
			Olive oil	+ 4°, - 6°	Non-drying
Linolenin.....	liquid	Linseed oil	- 20°, - 27°	Drying
Iso-linolenin.....	liquid	Hemp oil	- 15°, - 28°	Drying
			Poppy oil	- 18°	Drying

AND FATTY ACIDS

Acid	M.P.	B.P.	Solubility in water	Volatility	Reaction with Halogens
<i>Saturated Series</i>					
Butyric, C_4H_7COOH	-2°	162°	Soluble	Vol. 285°	No reaction
Caproic, $C_6H_{11}COOH$	-1.5°	235°	Insol.	No reaction
Caprylic, $C_7H_{13}COOH$	16.5°	236°	Sol. hot	No reaction
Capric, $C_8H_{17}COOH$	30°	268°	Sl.-sol.	No reaction
Lauric, $C_{11}H_{23}COOH$	43°	225°	Insol.	Vol. steam	No reaction
Myristic, $C_{13}H_{27}COOH$	53.8°	196° (15 mm.)	Insol.	Sl.-vol.	No reaction
Palmitic, $C_{16}H_{31}COOH$	62°	339°	Insol.	Non-vol.	No reaction
Stearic, $C_{17}H_{35}COOH$	69.2°	359°	Insol.	Non-vol.	No reaction
Arachidic, $C_{19}H_{39}COOH$...	75°	Insol.	Non-vol.	No reaction
<i>Unsaturated Series</i>					
Hypogæic, $C_{16}H_{31}COOH$..	33°	Insol.	Non-vol.	Adds 2Br
Oleic, $C_{17}H_{33}COOH$	14°	250°	Insol.	Vol. 250°	Adds 2Br
Linoleic, $C_{17}H_{31}COOH$	liquid at -18°	Insol.	Non-vol.	Adds 4Br
Linolenic, $C_{17}H_{29}COOH$...	} liquid	Insol.	Non-vol.	Adds 6Br
Iso-linolenic, $C_{17}H_{29}COOH$					

regard to these analytical reactions and the methods for their application such books as, **Lewkowitsch**, "Fats, Oils and Waxes," may be consulted.

Physical Constants

Specific Gravity.—The physical constants of fats and oils are often used for purposes of identification. Those most commonly used are, *specific gravity*, *melting point* or *solidification point*, *refractive index* and *viscosity*. The specific gravity may be most readily determined, in the case of oils or easily melting fats by means of an immersion hydrometer. It may also be determined more accurately by use of a specific gravity bottle or picnometer. The specific gravity of some oils may be cited as follows:

Oil	Sp. Gr.	Oil	Sp. Gr.
Olive oil.....	0.915 (at 15°)	Linseed oil (boiled)...	0.945 (at 15°)
Almond oil.....	0.917 (at 15°)	Palm oil.....	0.932
Peanut oil.....	0.919 (at 15°)	Cocoa butter.....	0.960
Cotton seed oil.....	0.923 (at 15°)	Cod liver oil.....	0.926
Sun-flower oil.....	0.925 (at 15°)	Butter fat.....	0.868 (at 100°)
Poppy seed oil.....	0.926 (at 15°)	Lard.....	0.859 (at 100°)
Hemp seed oil.....	0.928 (at 15°)	Tallow.....	0.857 (at 100°)
Linseed oil (raw).....	0.934 (at 15°)	Cocoanut oil.....	0.871 (at 100°)

Melting Point, Titer.—The *melting point* of fats and oils is determined by means of simple apparatus similar to that used in determining the melting point of organic compounds. In many cases the temperature at which the melted fat or liquid oil solidifies is determined, and this is called the *solidification point*. As there is considerable variation in the melting point or solidification point of most fats it has been found that the *solidification point of the mixed free acids* is a better constant. The fat is saponified and then the acids are set free by acidifying the saponification liquid. The solidification point of the mixed acids is then determined. This solidification point is known as the *titer*. The more common fats melt at temperatures ranging from 20° to 49°, cocoanut oil being the most liquid and tallow the most solid. Of the oils, linseed oil is the most difficultly solidified, at -20° to -27°, while olive oil is the most easily solidified, at +4° to -6°.

Fat	M.P.	Oil	S.P.
Tallow.....	36°-49°	Olive oil.....	+ 4° to - 6°
Lard.....	28°-45°	Peanut oil.....	- 5°
Laurel oil.....	32°-36°	Cotton seed oil.....	+ 1° to - 10°
Palm oil.....	27°-42°	Almond oil.....	- 10° to - 20°
Butter fat.....	29°-35°	Sun-flower oil.....	- 15° to - 18°
Cocoa butter.....	30°-34°	Poppy seed oil.....	- 18°
Cocoanut oil.....	20°-28°	Hemp seed oil.....	- 15° to - 28°
		Linseed oil.....	- 20° to - 27°

Table XV shows that when the melting point of the principal ester present in an oil is known the melting point of the fat is considerably lower. This is due to the fact that in these fats a considerable quantity of olein is also present which lowers the melting point. On account of the properties of palmitin and stearin, on the one hand, and of olein and the other unsaturated esters, on the other, it may be said, in general, that the larger the proportion of the former, which is present in a fat, the more solid will the fat be, while, if the proportion of olein is larger the fat will be more liquid in character. It will be observed, also, that there is considerable range between the minimum and maximum figures, both in the case of the specific gravity and also of the melting point. This is readily understood when we consider the nature of the fats and oils as mixed bodies, more or less variable in the condition in which they are obtained from their natural sources.

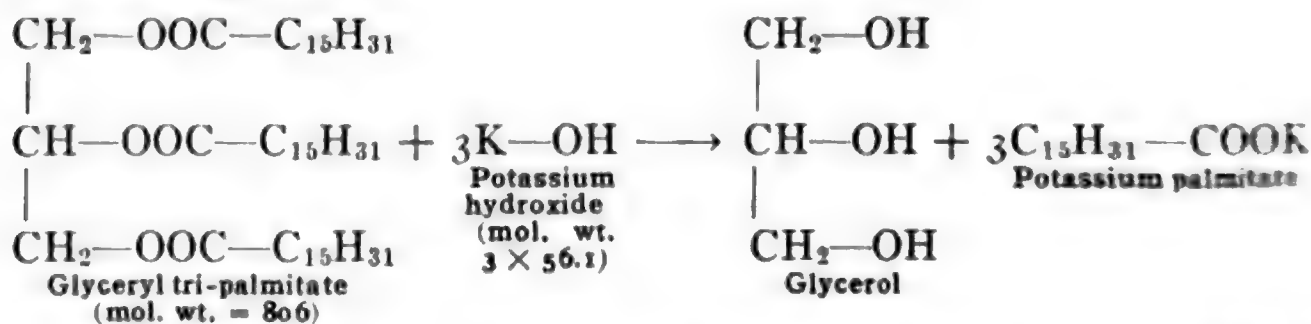
Refractive Index, Refractometers.—The *refractive index* of a fat or oil is the angle through which light is bent or refracted by passing through a thin film of the oil. The physical instrument which is used in measuring this angle is called a *refractometer*. The instrument is so constructed that a drop of oil is spread as a film between two prisms and the light passes through this film into the eye piece of the instrument. With oils which are liquid at ordinary temperatures no temperature controlling device is necessary but with fats it is necessary to have the prisms surrounded by a jacket containing water at a raised temperature. The most universal type of such an instrument either plain or jacketed is the **Abbe or Abbe-Zeiss refractometer**. On this instrument the scale reads the index of the refraction directly. A modified form of such a refractometer devised for use especially with butter is known as the *butyro-refractometer*. On this instrument the scale is in arbitrary

units covering the range of butter, lard and their substitutes. Another form of instrument, the *oleo-refractometer*, measures the comparative refraction of two oils at the same time the light passing through two small cylinders filled with oil one being a pure known oil as standard and the other an unknown oil for comparison. Still another modification is one known as the *immersion refractometer*. As its name indicates it is used by immersion in the liquid under examination. It has the advantage of being able to be used not only with emulsions of fats, but also to determine the strength of a large variety of solutions such as; milk serum (whey); acid, alkali and salt reagents; alcohol; sugar solutions, etc. The scale on this refractometer is also arbitrary but the readings may be readily converted into refractive indices by the use of tables.

Viscosity.—The *viscosity* of a melted fat or an oil may be defined as the friction which the particles exert upon each other in moving. It is usually determined by observing the flow of the oil through a capillary tube. The specific viscosity of an oil is the rate of flow compared with water, but in practice the viscosity is usually compared with that of some oil which has been taken as a standard. The oil commonly used as such a standard is *rape oil*. In this case the viscosity of the rape oil is considered as 100.

Chemical Constants

Saponification Number, Koetstorffer Value.—When an ester is saponified the reaction is quantitative. In the case of a pure glycerol ester, *e.g.*, glyceryl tri-palmitate, saponification is in accordance with the following reaction:



From the molecular weights of 806 for glyceryl tri-palmitate and of 56.1 for potassium hydroxide, the mass proportions are:

Glyceryl tri-palmitate: Potassium hydroxide: : 806 : 168.3

Taking the mass of glyceryl tri-palmitate as 1.00 the mass of potassium hydroxide becomes 0.2088. That is, to saponify 1.00 gm. of pure ester will require 0.2088 gm. of potassium hydroxide. Expressing

this in milligrams we have 208.8 which represents the *number of milligrams of potassium hydroxide required to saponify 1.00 gm. of the fat*. This number is known as the *saponification number* or *saponification value* which may be defined as just stated. It is also known as the *Koetstorffer Value*, from the name the man of who devised it. In practice the saponification of a fat is effected by using a Normal, $\frac{N}{1}$, potassium hydroxide solution which contains, in 1.00 cc. 0.0561 gm. or 56.1 m. gm. of potassium hydroxide. If, then, for any weight of fat taken, the number of cubic centimeters of $\frac{N}{1}$ KOH required is multiplied by 56.1 and the product divided by the number of grams of fat, the result will be the saponification value, *i.e.*;

$$\text{Saponification Value} = \frac{\text{cc. } \frac{N}{1} \text{ KOH} \times 56.1}{\text{Weight of fat in grams}}$$

The saponification values of a few of the pure esters and a few fats and oils are:

Esters	Sap. Val.	Fats	Sap. Val.
Butyrin.....	557.3	Butter fat.....	227.0
Palmitin.....	208.8	Palm oil.....	196.0-202
		Lard.....	195.4
Stearin.....	189.1	Beef tallow.....	193.2-200
Olein.....	190.4	Olive oil.....	185.0-196
Linolein.....	191.7	Linseed oil.....	192.0-195

Bromine or Iodine Value, Hübl-Wijs.—Another important chemical constant of fats and oils is one which depends upon the nature of the acid present as an ester. The acids present as esters in fats and oils are of two different classes, *viz.*, those belonging to the *saturated series* and those belonging to the *unsaturated series*. We have shown that the distinguishing reaction of these two series of compounds, both in the hydrocarbons and the various classes of their derivatives, is, that *unsaturated compounds take up halogen directly* with the formation of *addition products*. It has been found that the glycerol esters of the unsaturated acids form addition products readily, under certain conditions. If, therefore, a fat takes up bromine or iodine directly an ester of an unsaturated acid must be present. The determination of the

amount of halogen thus taken up will show us the amount of the unsaturated ester provided that we know which particular acid is represented. The unsaturated acids which occur as esters in fats and oils as has been previously stated, belong to three groups, viz., the **oleic acid** group, $(C_nH_{2n-2})O_2$, the **linoleic acid** group, $(C_nH_{2n-4})O_2$, and the **linolenic acid** group, $(C_nH_{2n-6})O_2$ (p. 181). The amount of halogen taken up, in the formation of addition products, depends upon the amount of the unsaturation, *i.e.*, the number of double or triple bonds, as indicated by the lower hydrogen content. **Oleic acid**, with *one double bond*, takes up *two halogen atoms* (bromine or iodine) per molecule of the acid. **Linoleic acid**, with *two double bonds* takes up *four halogen atoms* per molecule and **linolenic acid**, with *three double bonds*, takes up *six halogen atoms* per molecule. The esters, tri-olein, tri-linolein, and tri-linolenin, being tri-acid esters, will, of course, take up, per molecule, *three times* as much halogen as given above for the corresponding acid. According to the following proportions the amount of iodine theoretically absorbed by the three most common unsaturated acids may be readily calculated, as follows:



Oleic acid

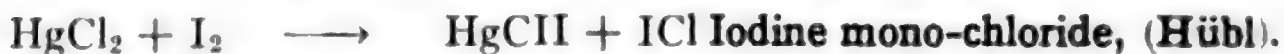


Linoleic acid



Linolenic acid

Therefore, *the amount of iodine, in grams, absorbed by 100 grams of the acid*, is, for these three acids, respectively, 90.07, 181.42, 274.1. These numbers are known as the iodine values, also as, the **Hübl**, or **Wijs** numbers, from the names of men who devised the two most accurate methods of determination. In practice, iodine is used more often than bromine. The form in which the iodine is used is that of iodine mono-chloride, ICl , or iodine tri-chloride, ICl_3 . The first is made by mixing a solution of iodine and mercuric chloride,



The iodine tri-chloride solution is made by the addition of chlorine to an iodine solution,



The iodine mono-chloride solution is the **Hübl** solution, the iodine tri-chloride solution, is the **Wijs** solution. In either case, the **exact**

strength of the solution, in terms of iodine, is determined by titration. The iodine solution is added to the fat or acid dissolved in chloroform or carbon tetra-chloride, and the absorption allowed to take place. After the absorption is completed the excess of iodine is determined by titration and the amount actually absorbed is calculated *per 100 grams of the fat* or acid used. The iodine values, as thus determined, for some of the common fats and oils are given in the following table. It will be noticed that, with the exception of cocoanut oil and cocoa butter, *butter fat has the lowest value* of the common fats and oils.

Pat or oil	Iodine value	Pat or oil	Iodine value
Linseed oil.....	173-201	Laurel oil.....	68.0-80.0
Hemp seed oil.....	148	Palm oil.....	51.5
Poppy seed oil.....	133-143	Cocoa butter.....	32.0-41.0
Sun-flower oil.....	119-135	Cocoanut oil.....	8.0-9.5
Maize oil.....	111-130	Human fat.....	58.9-73.3
Cotton seed oil.....	108-110	Lard.....	50.0-70.0
Almond oil.....	93-97	Beef tallow.....	38.0-46.0
Peanut oil.....	83-100	Butter fat.....	26.0-38.0
Olive oil.....	79-88		

Insoluble Acids, Hehner Value.—The acids which are set free from the fat or oil by saponification and subsequent acidification, differ in two other respects as well as in their power to absorb halogens. These are, (1) *solubility*, (2) *volatility*. Some of the acids, like **butyric**, are *soluble in water* while most of them are insoluble. Some, like **butyric** and **lauric**, are *volatile with steam*, others are non-volatile. The determination of the amount of insoluble acids in a fat gives us a value known as the **Hehner Value** which may be defined as *the sum of the insoluble acids and unsaponifiable matter in a fat expressed in per cent.* After saponification of the fat the soap solution is acidified and the insoluble fatty acids are collected on a filter paper and weighed. In the case of most of the common fats and oils the Hehner value lies in the neighborhood of 95, with butter fat as the striking exception, with a value of *less than 90*. The Hehner values which differ much from 95 are given in the table at the end of this section.

Volatile Acids or Reichert-Meissl Value.—The separation of the *volatile* from the non-volatile acids is accomplished by distillation of the mixed fatty acids after they have been set free from the saponifica-

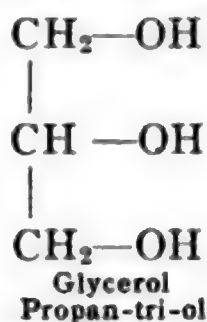
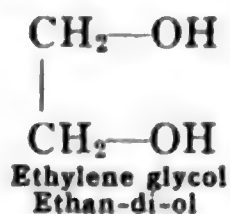
tion liquid by acidifying. The **Reichert-Meissl Value** may be defined as, *the number of cubic centimeters of one-tenth normal potassium hydroxide required to neutralize the volatile fatty acids, obtained from 3.0 grams of a fat or oil by the Reichert distillation process.* This determination does not yield absolute values but is of considerable importance, especially in the examination of butter and its imitations. Some of the values which have been obtained, will be found in the table preceding. It will be seen that *butter fat alone has a value which is at all high.* This is natural as it is the only one which has a large amount of butyric acid. The composition of **butter fat** may be given in this connection. As recently determined by **E. B. Holland** of the **Massachusetts Experiment Station**, the acids present are as follows. (*Mass. Exp. Sta. Bul.*, 166; 1915).

COMPOSITION OF BUTTER FAT

Volatile Acids		Non-volatile Acids	
Butyric	3.2 per cent.	Lauric	1.9 per cent.
Caproic	1.4 per cent.	Myristic	22.6 per cent.
Caprylic	1.0 per cent.	Palmitic	19.3 per cent.
Capric	1.8 per cent.	Stearic	11.4 per cent.
		Oleic	27.4 per cent.

C. HIGHER POLY-HYDROXY ALCOHOLS

The di-hydroxy and the tri-hydroxy derivatives of the saturated hydrocarbons which have been studied thus far are:

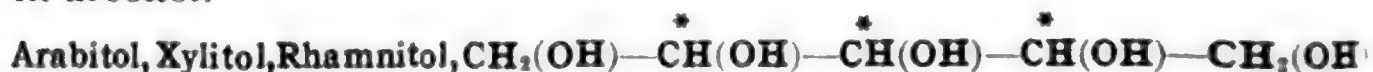


As previously stated, it is generally true that stable compounds do not result when more than one hydroxyl group is linked to one carbon atom. It is plain therefore that the simplest member of each class of poly-hydroxy substitution products must have as many carbon atoms as there are hydroxyl groups. Thus, the simplest di-hydroxy compound is the di-hydroxy ethane, glycol, and similarly, the simplest tri-hydroxy compound is the tri-hydroxy propane, or glycerol, as above. Considering, now, those poly-hydroxy substitution products

which contain more than three hydroxyl groups, we find that compounds are known with *four, five, six, seven, eight, and nine*. These compounds all agree with the statements just made and the constitution of each has been fully established. In connection with them, two general facts are of importance. *First*, they are all *true alcohols*, being a combination of primary and secondary alcohols, as has been explained under glycerol. When oxidized, therefore, two different series of compounds are possible. The primary alcohol groups, which are always the end carbon groups, are oxidizable to aldehyde and then to acid groups. The secondary alcohol groups which include all of the intermediate carbon groups, are oxidizable to ketone groups (p. 121). The oxidation products of these poly-hydroxy alcohols lead directly to the very important group of compounds known as the **carbohydrates**, or **sugars**, to be studied later. As was mentioned, in connection with glycol and glycerol, the increased substitution of the hydroxyl group into a hydro-carbon chain, confers upon the compound a sweet taste. The compounds following, viz., **erythritol**, **arabitol**, **mannitol**, etc., all possess a sweet taste. *Second*, the second general fact is, that in all of these higher hydroxy compounds we have *more than one asymmetric carbon atom*, as indicated by the * in the formulas. This makes possible the existence of these compounds in several *stereo-isomeric forms*, which will be discussed at length when we consider the carbohydrates.



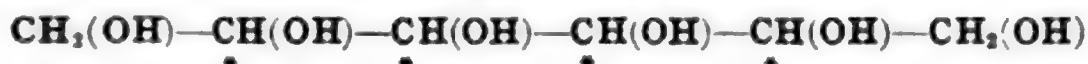
The tetra-hydroxy compound, viz., **tetra-hydroxy butane**, or **1-2-3-4-butan-tetr-ol**, is known as **erythritol** or **erythrite**. It occurs free in nature in certain algæ and also as **erythrin**, an ester of an aromatic acid, in certain lichens. It is a crystalline substance, melting at 126° and boiling at 329°. It is easily soluble in water and slightly in alcohol.



The penta-hydroxy compound, viz., **penta-hydroxy pentane**, or **1-2-3-4-5-pentan-pent-ol**, is known as **arabitol** or **arabite**. It occurs also in stereo-isomeric forms as **xylitol**, and **rhamnitrol**. The formula is as above. The names of these three isomers are derived from the substances or compounds from which they are obtained. Arabitol is obtained from **arabinose** which is found in gum ara bic. Xylitol is

similarly related to **xylite**, a woody cellulose, and rhamnitol to **rhamnose** a sugar. The first of these melts at 102° , the second has not been crystallized and the third melts at 121° . They are all soluble in water.

Mannitol, Dulcitol, Sorbitol



The hexa-hydroxy compound, viz., **hexa-hydroxy hexane**, or **1-2-3-4-5-6-hexan-hex-ol**, with the formula as above, exists in different stereoisomeric forms, the three most common ones being known as **mannitol** or **mannite**, **dulcitol** or **dulcite**, and **sorbitol** or **sorbite**. Mannitol is found quite widely distributed in nature. Its chief source is the juice of the manna ash tree (*Fraxinus Ornus*). The juice is dried or coagulated and the residue, known as *manna*, yields about 30-60 per cent. of mannitol. The manna is sweet and edible. This manna is not the one mentioned in the Bible as that was probably an edible lichen (*Sphaerothallia esculenta*), which grows upon a tamarix tree (*Tammerix gallica*, var. *mannifera*). This last manna contains a sugar, but no mannitol. Mannitol is also found in a toad-stool (*Agaricus integer*), and amounts to about 20 per cent. of the dry substance. It is present in small amounts in celery, syringa leaves, olives, etc. It also occurs in rye bread. From water mannitol crystallizes in prisms but from alcohol in needles. It is soluble in six parts of water. It melts at 165° and in water solution it is levo rotatory. The synthesis of mannitol involves its relation to the sugars and will not be considered at this time. The same is true in regard to the oxidation products. The other two hexa-hydroxy alcohols, mentioned above, are stereo-isomeric with mannitol. They resemble it in chemical properties differing from it physically, especially in optical properties. Dulcitol, is inactive, while sorbitol is levo rotatory like mannitol. The different stereo-chemical structures for these, and the other isomeric hexa-hydroxy alcohols, will be explained when the stereo-isomerism of the carbohydrates is considered. Suffice it to say at this time that there are possible *ten isomeric compounds* of the same structure as mannitol. Dulcitol is found in nature in a manna from Madagascar and in some plants. It crystallizes in columns which melt at 188.5° . It is less soluble in water than mannitol. Sorbitol is found in the berries of the mountain ash tree, in pears, plums, cherries, apples, etc. It crystallizes from water in fine needles which melt at 110° - 111° .

VIII. MIXED POLY-SUBSTITUTION PRODUCTS

GENERAL

Thus far, in considering the poly-substitution products, resulting from the substitution of more than one mono-valent element or radical for an equivalent number of hydrogen atoms, we have spoken of those compounds in which the two or more substituting groups are the same, viz., poly-halogen compounds, poly-alcohols, poly-amines, etc. Having just considered the poly-alcohols it would seem natural that the next step would be to study similar compounds containing more than one aldehyde or acid group, *i.e.*, poly-aldehydes and poly-acids. Before we take up these last two groups of compounds, however, it seems better to consider, those poly-substitution products in which the substituting groups are different. It is plain that a great variety of mixed compounds are possible as, theoretically, we may have any combination of two or more different substituting elements or groups which are capable of forming substitution products. In many cases of compounds which are not important we shall simply give their formulas and names as examples without further description.

A. MIXED HALOGEN AND CYANOGEN COMPOUNDS

Halogens Only.—In the group of mixed poly-halogen compounds we may have di-substitution products like **di-chlor methane**, CH_2Cl_2 , such as CH_2ClBr , **brom chlor methane**, CH_2BrI , **brom iodo methane**, etc.; tri-substitution products like **chloroform**, CHCl_3 , *e.g.*, CHCl_2Br , **brom di-chlor methane**, CHClBr_2 , **di-brom chlor methane**, CHCl_2I , **di-chlor iodo methane** etc., and tetra-substitution products like **carbon tetra-chloride**, CCl_4 , such as CCl_2I_2 , **di-chlor di-iodo methane**, etc. These are all derivatives of methane but analogous derivatives of other hydrocarbons are known.

Halogen and Nitro Group.—**Chlor Picrin.**—We may also have mixed compounds containing halogen elements and some non-halogen element or group such as the nitro group. An example of this is **chlor picrin** so named because it is made by the chlorination of **picric acid**, a **benzene**

compound (Pt. II). Its formula is $\text{CCl}_3(\text{NO}_2)$. It is thus related to chloroform and is known also as **nitro chloroform**. It is a liquid, b.p. 112° , with an extremely bad odor and a very irritating action upon eyes and mucous membranes. It is one of the so-called *war gases* and was one of two or three most extensively used in the late war.

Halogens and Amino Group.—Mixed compounds containing both halogens and amino groups may be illustrated by the following: $\text{CH}_2\text{Br}-\text{CH}_2-\text{NH}_2$, **1-amino 2-brom ethane**, $\text{CH}_3-\text{Cl}_2-\text{NH}_2$, **1-amino 1-di-iodo ethane**, $\text{H}_2\text{N}-\text{CH}_2-\text{CHCl}-\text{CH}_2-\text{NH}_2$, **2-chlor, 1-3-di-amino propane**.

Halogens and Cyanogen Group.—Compounds containing both halogens and the cyanogen group are *nitriles of halogen acids*. They may be considered as derivatives of hydrogen cyanide, $\text{H}-\text{CN}$, or of cyanogen, $\text{NC}-\text{CN}$. The simplest compounds of this kind contain no other carbon than the cyanogen carbon, *e.g.*, **chlor cyanogen**, $\text{Cl}-\text{CN}$, **brom cyanogen**, $\text{Br}-\text{CN}$, and **iodo cyanogen**, $\text{I}-\text{CN}$. These are nitriles of the corresponding halogen formic acids. Halogen derivatives of alkyl cyanides may be illustrated with those related to methyl cyanide or acetic nitrile, CH_3-CN .

$\text{CH}_2\text{Cl}-\text{CN}$	CHCl_2-CN	CCl_3-CN
Chlor methyl cyanide	Di-chlor methyl cyanide	Tri-chlor methyl cyanide
Chlor acetic nitrile	Di-chlor acetic nitrile	Tri-chlor acetic nitrile

Cyanogen and Amino Compounds.—**Cyan-amide.**—As derivatives also of hydrogen cyanide or of cyanogen and likewise as derivatives of ammonia or of amines are compounds containing both a cyanogen and an amino group. The most important representative of this kind is a compound known as **cyan-amide**, $\text{NC}-\text{NH}_2$. This compound will be considered later with other cyanogen compounds (p. 422). Analogous to cyan-amide are corresponding alkyl amino compounds, *e.g.*, **cyan methylamine**, $\text{NC}-\text{NH}(\text{CH}_3)$, and **cyan di-ethyl amine** $\text{NC}-\text{N}(\text{C}_2\text{H}_5)_2$.

In all of these mixed compounds, the substances possess the properties of *both kinds of substitution products* represented. The halogen nitro compounds, on reduction, yield halogen amines. The halogen amines are basic compounds, like the amines themselves, and form salts with mineral acids. The halogen cyanogen compounds possess the nitrile properties of alkyl cyanides, and on hydrolysis yield halogen acids. The cyanogen amines are, similarly, both acid nitriles and

amine bases. Thus we could expand this class of compounds almost indefinitely, but that is unnecessary, in our present study. Any particular compound which is of importance, in connection with other compounds, will be taken up in the proper place.

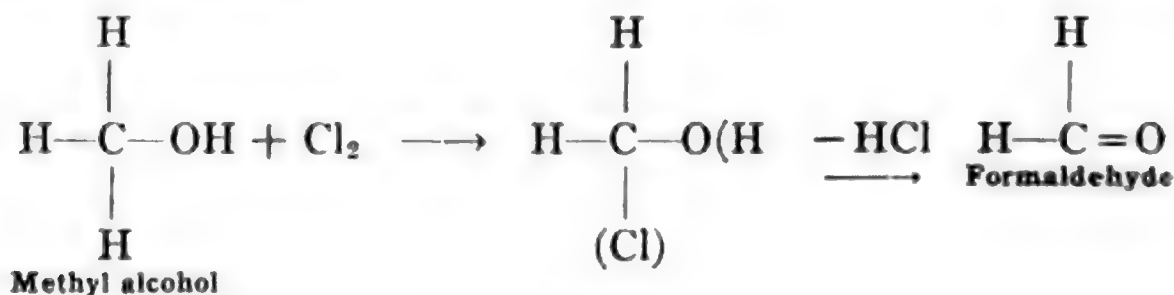
B. MIXED HYDROXY COMPOUNDS—SUBSTITUTED ALCOHOLS

I. HALOGEN-ALCOHOLS

The most important derivatives of this mixed type are those obtained by substituting, in alcohols, aldehydes, or acids, some other element or group. This gives us compounds known, in general, as *substituted alcohols*, *substituted aldehydes*, and *substituted acids*. These three classes of mixed compounds will now be considered. The simplest group of substituted alcohols are the halogen alcohols. Of the halogen alcohols the simplest would be derived from methyl alcohol, *e.g.*,



Such a compound, however, if produced by the action of chlorine upon methyl alcohol, evidently splits off hydrochloric acid and yields an aldehyde, as follows:

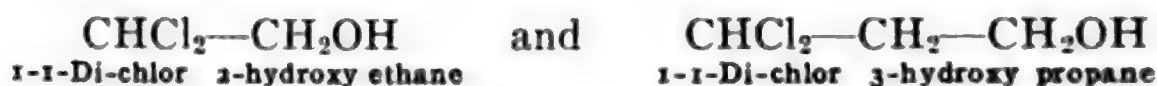


That is, the action of chlorine, in such cases, is simply oxidation, through loss of hydrogen, the alcohol being oxidized to an aldehyde. The reaction, as given above, does not take place with methyl alcohol, but does occur in the case of ethyl alcohol when it is treated with chlorine in the manufacture of chloroform (p. 183). In general, this result is always obtained when alcohols are treated with halogens. The carbon group affected by the halogen is always that one which contains the hydroxyl group. This gives a carbon group having both a halogen and hydroxyl present in it and such a grouping, being, evidently un-

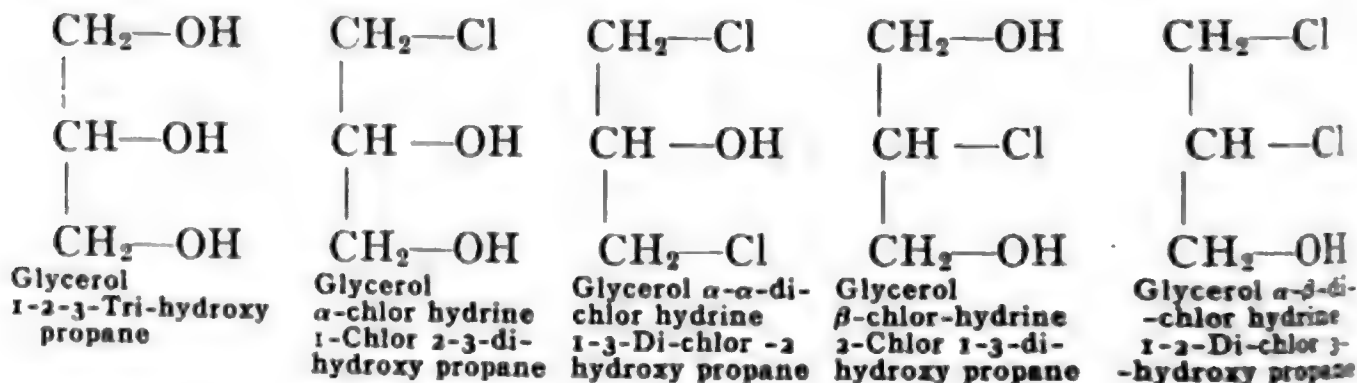
phorus halogen compounds, *e.g.*, phosphorus tri-chloride, PCl_3 , or tri-bromide, PBr_3 , etc., one of the hydroxyl groups is replaced by a halogen atom, yielding a compound known as a halogen-hydrine. These compounds are plainly mono-esters of the poly-hydroxy alcohol and the halogen acid and have been previously referred to (p. 201).



More than one hydroxyl may be thus replaced and the resulting compounds are known as, di-halogen hydrines, tri-halogen hydrines, etc., depending upon the number of halogens introduced. The compound given above is, glycol chlor hydrine. Considering these halogen-alcohol compounds as derivatives of the mono-hydroxy alcohols we have other known compounds in which more than one halogen is introduced into the non-hydroxy carbon group, *e.g.*;



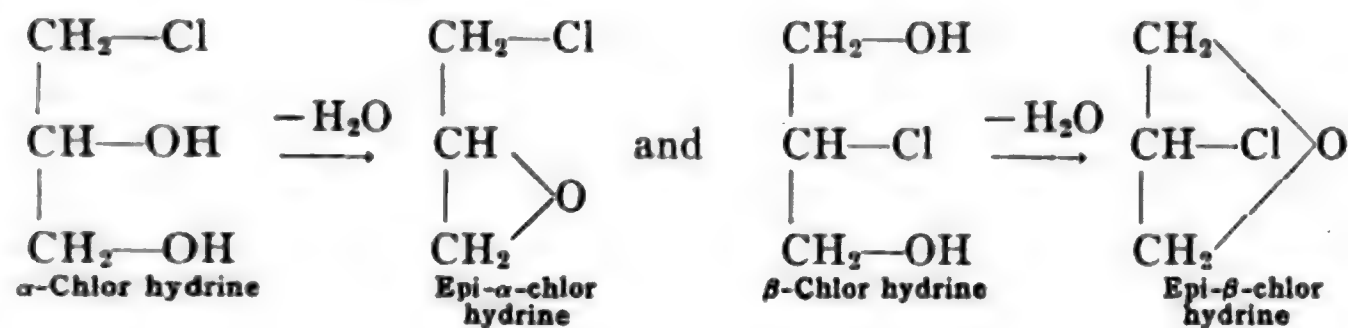
From the higher poly-hydroxy alcohols similar halogen-alcohols are obtained, which are known, also, as halogen-hydrines, *e.g.*;



The chlor-hydrines are especially important in synthetic reactions which we shall use later.

Epi-chlor Hydrines.—An important reaction takes place with mono-chlor hydrines which contain at least two remaining hydroxyl groups, as, *e.g.*, those derived from glycerol. The mono-chlor hydrines lose water and are converted into anhydrides known as **epi-chlor hydrines**. The reactions take place most readily with the *alpha*-chlor

hydrines, as in the first reaction, but also with the *beta*-compounds as in the second reaction.

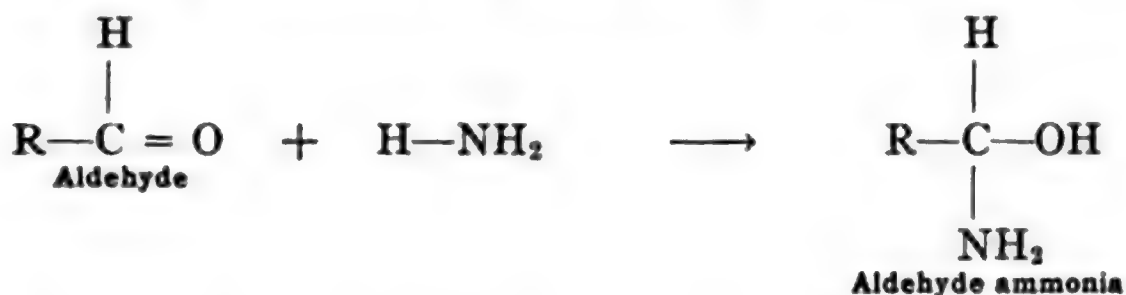


II. AMINO ALCOHOLS

From the chlor hydrines, by means of ammonia, we can pass to the corresponding *amino-alcohols*,



The most important reaction, however, for the formation of the amino alcohols, is that of ammonia and aldehydes, (p. 116).



In this case the amino group is united to the same carbon as the hydroxyl.

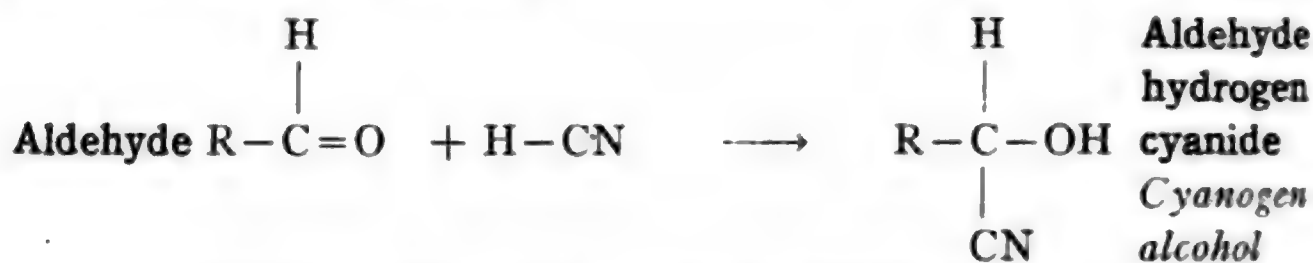
III. CYANOGEN ALCOHOLS

Cyanogen-hydroxyl Compounds.—The cyanogen-alcohols are very similar to the amino-alcohols in their methods of formation. They may be formed from the chlor-hydrines by the action of potassium cyanide, as follows:



In this case the cyanogen and hydroxyl groups are linked to different carbons. They may also be formed from the aldehydes by the addition

of hydrogen cyanide, in which case the cyanogen group is linked to the same carbon as the hydroxyl,



The cyanogen alcohols are nitriles of hydroxy acids.

C. SUBSTITUTED ALDEHYDES AND KETONES

I. HALOGEN ALDEHYDES

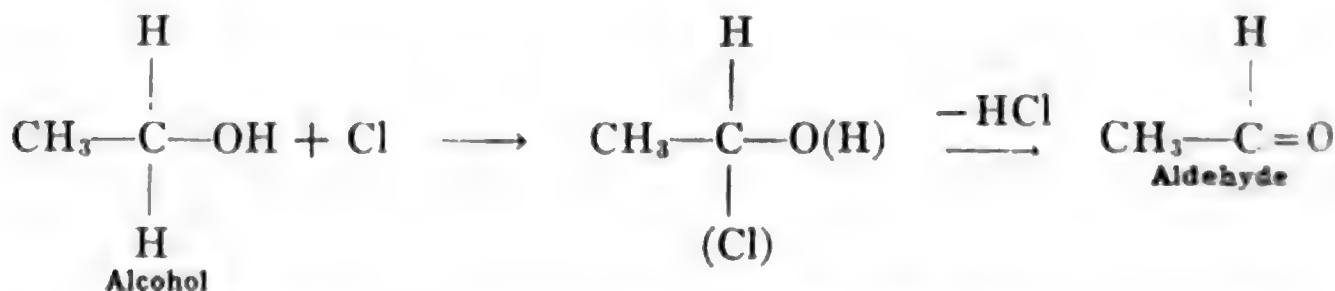
Tri-chlor Aldehyde CCl_3-CHO Chloral

When aldehydes are directly halogenated the halogen enters a carbon group other than the one containing the aldehyde group. In the case of acet-aldehyde chlorine may be substituted for all three of the hydrogens in the methyl radical and we obtain, **tri-chlor acet-aldehyde**:



It will be recalled that this compound is the intermediate product in the formation of chloroform from alcohol. The alcohol is first oxidized to aldehyde by means of chlorine, (p. 115), the substitution of chlorine in the aldehyde then taking place as above.

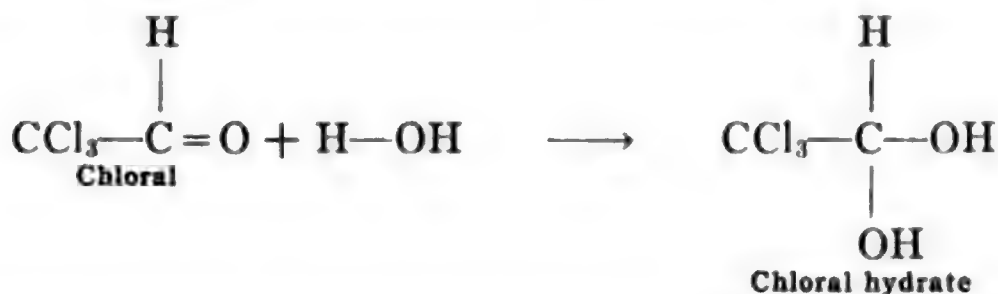
It is possible that this oxidation takes place by the loss of hydrogen through the direct action of chlorine without the action of oxygen (p. 222).



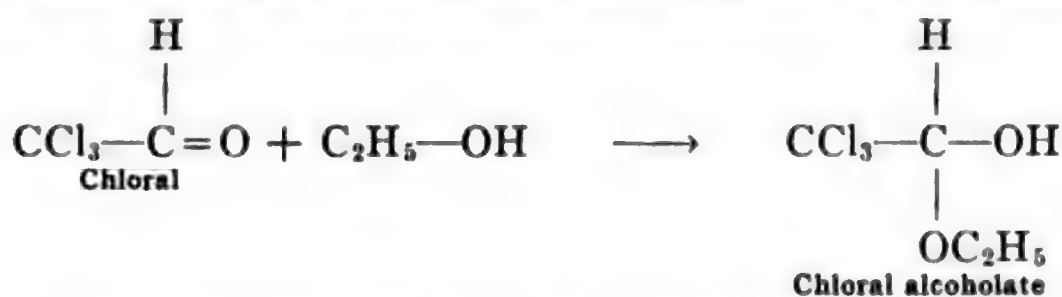
In the preparation of chloroform the **tri-chlor acet-aldehyde** then reacts with an alkali present yielding **chloroform** and the alkali-metal salt of **formic acid**, as follows:



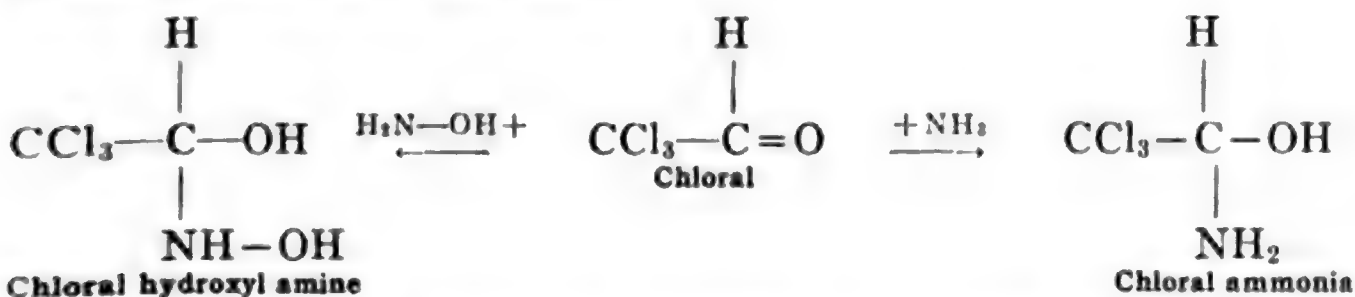
Chloral.—**Chloral**, or **tri-chlor acet-aldehyde**, was first prepared by **Liebig** in 1832 by the chlorination of alcohol as above. It may also be obtained by the direct action of chlorine upon acet-aldehyde. It is an oily liquid with a sweet suffocating odor. It boils at 97.7° . It does not mix with water but on boiling with water it forms a hydrated compound which crystallizes in large clear crystals, readily soluble in water. This is known as **chloral hydrate**. The structure of chloral hydrate is probably that of an addition product, viz., a chlorinated di-hydroxy alcohol. In this compound we have an exception to the general rule that two hydroxyl groups can not be linked to the same carbon atom.



This constitution of the hydrate is indicated by the fact that it does not give the aldehyde reaction with fuchsine as does both acet-aldehyde and chloral. Also by the fact that the ethyl ester of such a di-hydroxy alcohol is known and is formed from chloral by reaction with alcohol.



Similar addition products of chloral and ammonia and of chloral and hydroxyl amine are also known.

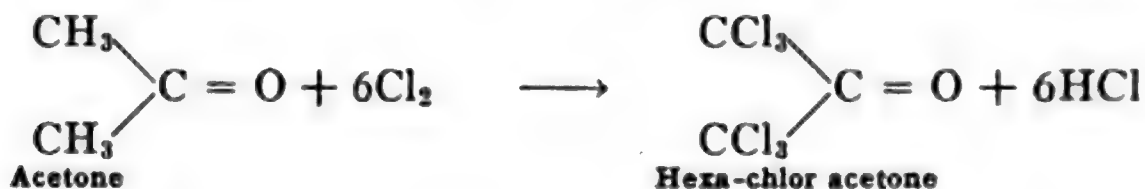


The formation of addition products with chloral is much easier than with acet-aldehyde itself, due to the influence of the three negative chlorine atoms in the alkyl radical. Chloral undergoes polymerization, as does acet-aldehyde, the product being **meta-chloral** $(\text{CCl}_3\text{CHO})_3$.

It reduces ammoniacal silver nitrate solution. It is oxidizable to **tri-chlor acetic acid** and, by the action of zinc and hydrochloric acid, is reduced to **acet-aldehyde**. Chloral is a most important soporific and is used in certain cases for anesthetic purposes. In this latter use it is always the readily soluble form of chloral hydrate which is employed. Its anesthetic action was, at first, attributed to the probable formation of chloroform but this is now doubted.

II. HALOGEN KETONES

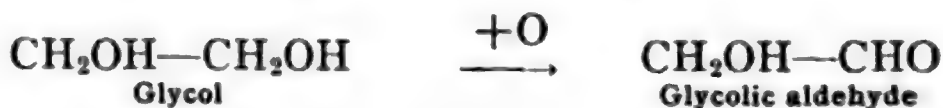
Halogen-ketones are similarly obtained by direct halogenation of ketones. In the case of acetone, or propanone, all six possible chlor acetones are known, and are obtained either by direct chlorination, or by other reactions, which we need not discuss here.



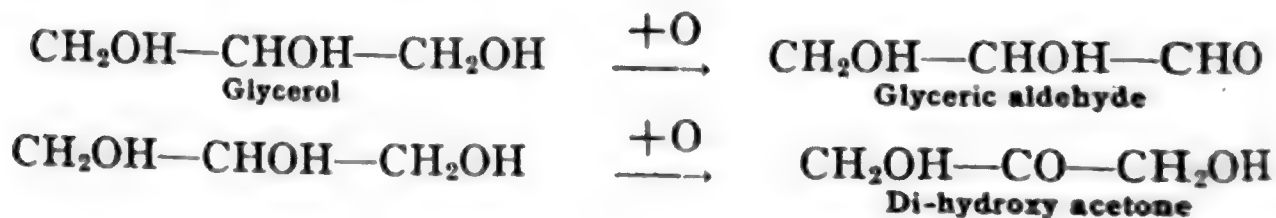
III. HYDROXY ALDEHYDES AND HYDROXY KETONES

When poly-hydroxy alcohols are oxidized the first product is a compound in which one of the alcohol groups has been oxidized either to aldehyde or to ketone depending on whether the alcohol group is primary or secondary.

Aldehyde Alcohols.—From the simplest poly-hydroxy alcohol **glycol** or **ethandiol**, the only product of this kind that is possible is an aldehyde-alcohol known as **glycolic aldehyde**.



Ketone Alcohols.—From the higher poly-hydroxy alcohols however, which contain both primary and secondary alcohol groups we obtain both *aldehyde alcohols* and *ketone alcohols*. **Glycerol** or **propantriol** thus yields the following:



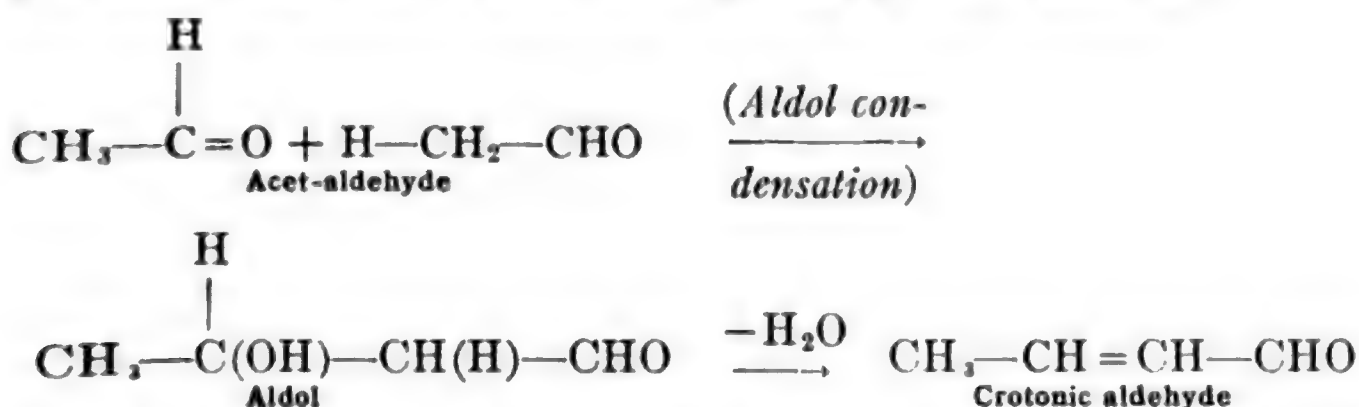
Both the hydroxy aldehydes or aldehyde alcohols and the hydroxy ketones or ketone alcohols undergo the characteristic aldehyde and ketone reactions due to the carbonyl group. They react with hydrogen cyanide, phenyl hydrazine and hydroxyl amine. These reactions have been discussed in connection with the aldehydes (pp. 116, 224) and will be considered again when we study the carbohydrates. The carbohydrates in fact belong here with these hydroxy aldehyde and hydroxy ketone compounds but on account of other relations they are better considered at a later time.

Glycolic Aldehyde $\text{CH}_2\text{OH}-\text{CHO}$. **Glyceric Aldehyde** $\text{CH}_2\text{OH}-\text{CHOH}-\text{CHO}$

The simplest member of the group, as given above, is known as **glycolic aldehyde** and is obtained only in the form of its water solution. It derives its name as do other aldehydes from the fact that it yields **glycolic acid** on oxidation. **Glyceric aldehyde** and **di-hydroxy acetone** the oxidation products of glycerol (p. 200) are very important as they together constitute the simplest sugar that is known and the first one synthesized (p. 320).

Aldol $\text{CH}_3-\text{CH}(\text{OH})-\text{CH}_2-\text{CHO}$. **β -Hydroxy Butyric Aldehyde**

This compound is an important and interesting member of the group. It is made by the condensation of two molecules of acet-aldehyde (p. 116). The reaction is, therefore, known as the *aldol condensation* and in its general form is characteristic of aldehydes taking place also with the hydroxy aldehydes, *e.g.*, with glycolic aldehyde,



Aldol is oxidizable to hydroxy butyric acid and, being a *beta-hydroxy* compound, loses water yielding an unsaturated aldehyde, **crotonic aldehyde** (p. 169), as in the second part of the reaction.

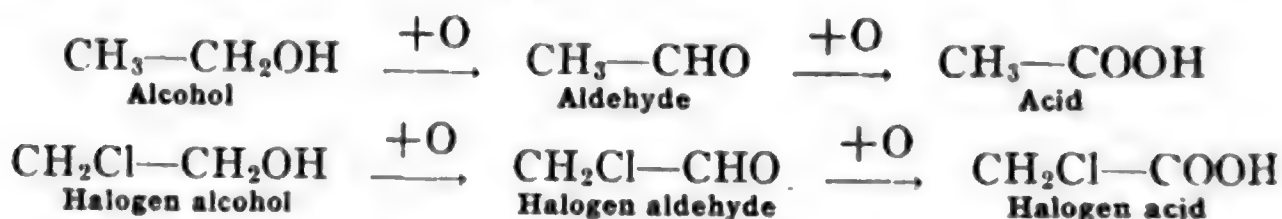
D. SUBSTITUTED ACIDS

The mixed compounds which we have been considering may be regarded as mono-substitution products of that class of compounds

characterized by the other group present. The chlor-hydrines, *e.g.*, may be regarded as chlorine substitution products of alcohols and similarly chloral, $\text{CCl}_3\text{—CHO}$, is a substituted aldehyde. We should expect, therefore, to have acids in which substitution of other groups or elements occurs giving the general group of compounds which we would designate as *substituted acids*. These are the compounds which we have now to consider and we shall naturally find different sub-classes corresponding to the different substitution products of the hydrocarbons themselves. We shall have to consider, then, as mixed acid compounds (a) *halogen acids*, (b) *amino acids*, (c) *cyanogen acids*, and (d) *hydroxy acids*, in all of which the other substituting group is different in character from the carboxyl group. The amino-acids will be discussed by themselves, later, as they are closely related to the proteins, which we do not wish to consider at this time. Similarly the cyanogen acids will not be taken up now, for they are plainly nitriles of the dicarboxy acids and on that account will be better considered directly in connection with these latter compounds. There remains, then, for discussion at this time the two classes of halogen acids and hydroxy acids.

I. HALOGEN ACIDS

The halogen acids, of course, bear the same relation to the halogen aldehydes and the halogen alcohols (halogen hydrines) that unsubstituted acids do to the unsubstituted aldehydes and alcohols. That is, they are the direct oxidation products.



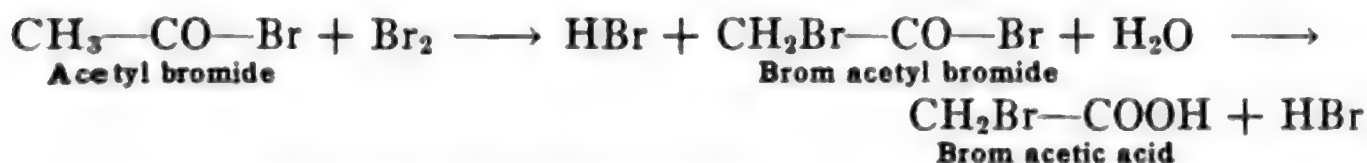
This reaction of oxidation often takes place, as has been referred to in the case of tri-chlor aldehyde, or chloral, which yields tri-chlor acetic acid on oxidation. But this is not the ordinary method of preparation of the halogen acids. The common method of preparing these compounds is by the direct halogenation of the acids themselves.

Halogenation of Acids.—Several facts are of especial importance in connection with the halogenation of the saturated acids. In most cases the introduction of the halogen element into the acid takes place with comparative ease. It may be by the direct action of the halogen,

(chlorine, for example) at ordinary raised temperatures, or by the action of the halogen in the presence of a carrier. It is also interesting that the higher the molecular weight of the acid, *i.e.*, the higher the acid stands in the homologous series, the more easily does substitution occur. For example, to form **brom acetic acid** it is necessary to heat acetic acid with bromine in a sealed tube for 100 *hours*. **Propionic acid**, however, is brominated by heating for 40 *hours*, while **butyric acid** requires similar heating for only 7 *hours*, in order to accomplish bromination. Such substitution of halogens takes place with the acids themselves, but still more easily with the *acid anhydrides* or the *acid chlorides*. The method of brominating most commonly used is to treat the acid with red phosphorus and then to add bromine. The first reaction is to form the acid bromide, (*e.g.*)



The bromine then acts directly upon the acid bromide forming brom acetyl bromide, which, by the action of water, is hydrolyzed yielding **brom acetic acid**, as follows:



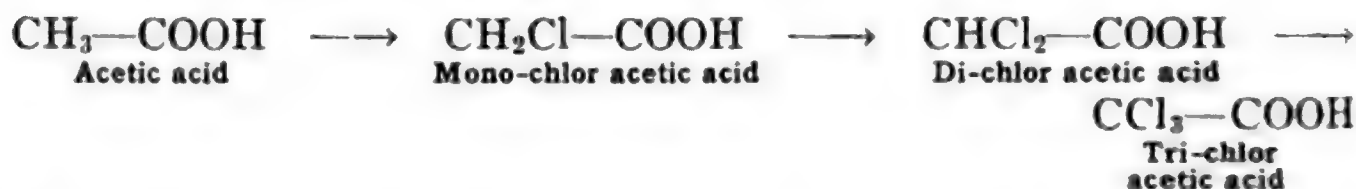
Nomenclature of Substituted Acids.—In the case of acids which contain more than two carbon groups the substitution may take place in any of the carbon groups other than the carboxyl. To distinguish these isomeric acids by name the position of the substitution is indicated by means of the Greek letters, *alpha* (α), *beta* (β), *gamma* (γ), *delta* (δ), *epsilon* (ϵ), etc., beginning with the carbon *adjoining the carboxyl group*. **Normal caproic acid** would thus have the different carbons designated as follows, $CH_3-CH_2-CH_2-CH_2-CH_2-COOH$.



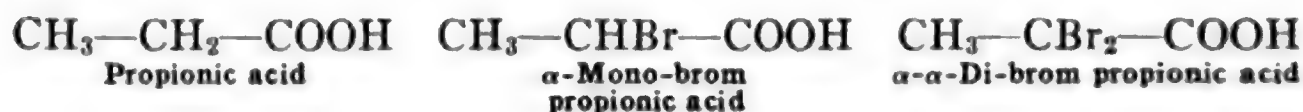
By the method of halogenation just described the halogen always enters the *alpha* position. In the case of isomeric branched chain compounds, in which the *alpha* carbon has no remaining hydrogen atom united to it, direct substitution does not take place. To form halogen acids from acids of this character other methods of preparation must be employed.

In case direct halogenation is continued for some time beyond

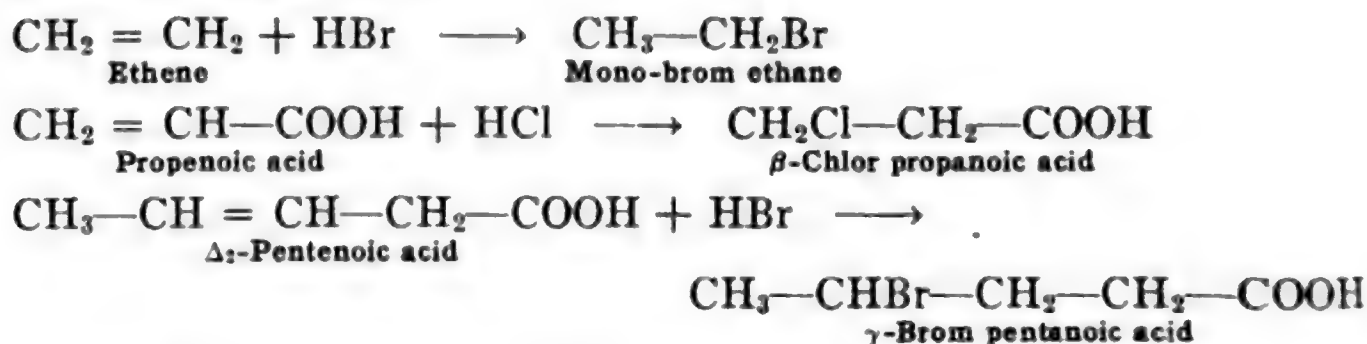
that required for substitution of one halogen atom, then more than one halogen is substituted up to the limit of the *alpha* carbon. Thus acetic acid yields, finally, tri-halogen acetic acid,



Propionic acid yields first the mono- and then the di-halogen propionic acid,



For the preparation of halogen acids in which the substitution is in the *beta* or *gamma* position the reaction of the unsaturated acids of the ethylene series is usually employed. As ethylene by the addition of hydrobromic acid yields brom ethane, so in like manner, *unsaturated acids of the ethylene series take up halogen acids* and pass to the *mono-halogenated saturated acid*,



By means of the similar reaction with halogens alone the unsaturated acids yield *di-halogen saturated acids*,

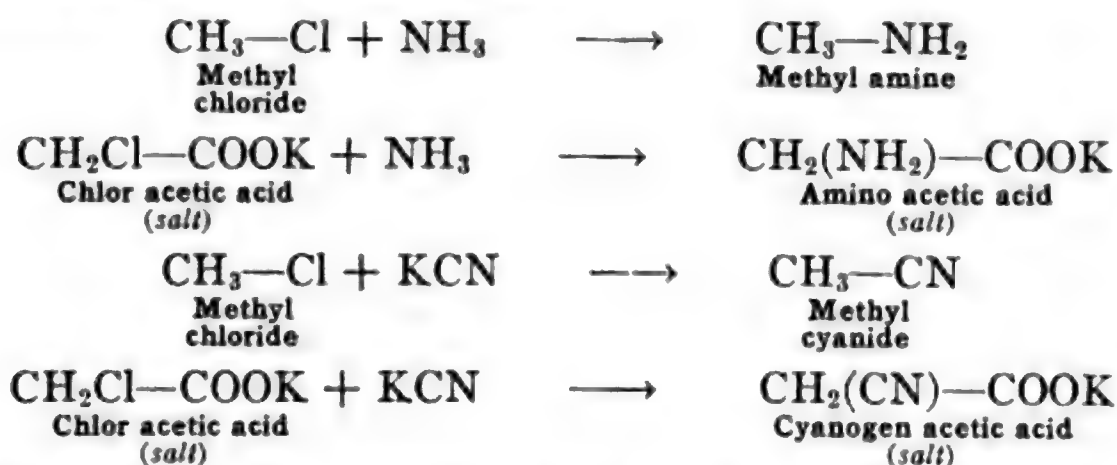


General Properties.—The halogen acids are characteristically acid compounds undergoing all acid reactions and yielding derivatives corresponding to the acid from which they are derived. They form, therefore, *anhydrides*, *salts*, *esters*, *acid chlorides*, and *acid amides*. In fact, the acid character of the halogen acids is *more pronounced* than that of the original unsubstituted acids themselves. This is due to the presence of the additional negative group, *i.e.*, the halogen containing group. Also, the more halogen atoms substituted the stronger is the acid property. This increasing acid character may be illustrated

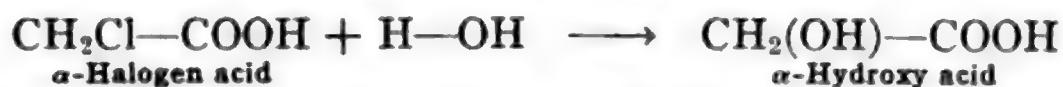
by giving the electric conductivity, or *dissociation constant*, of the halogen acetic acids.

Acid	Dissociation constant
$\text{CH}_3\text{—COOH}$ Acetic acid,	0.0018
$\text{CH}_2\text{Cl—COOH}$ Mono-chlor acetic acid,	0.1550
$\text{CHCl}_2\text{—COOH}$ Di-chlor acetic acid,	5.1400
$\text{CCl}_3\text{—COOH}$ Tri-chlor acetic acid,	121.0000

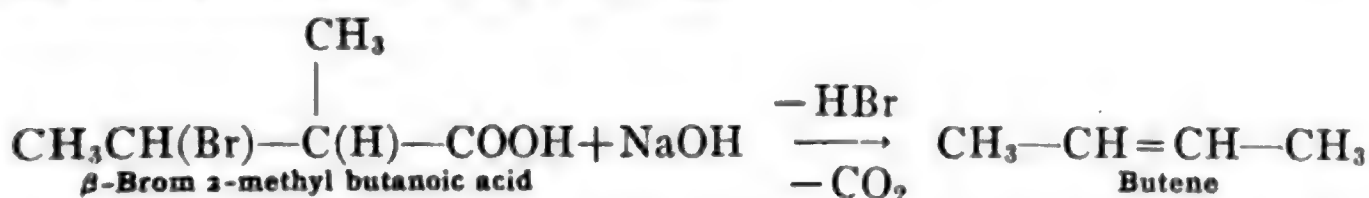
Reactions.—The halogen acids react also like alkyl halides. With ammonia they yield *amino acids*, and with potassium cyanide the products are *cyanogen acids*, or *nitriles*.



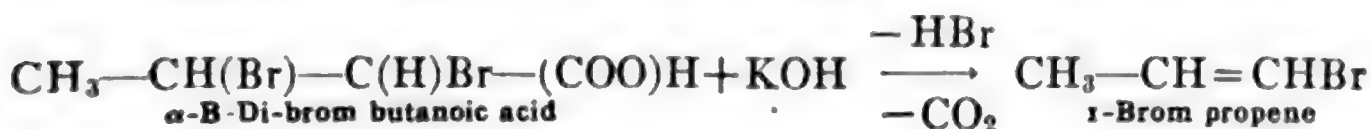
Alpha-, Beta-, and Gamma-Acids.—The replacement of the halogen by hydroxyl takes place readily in the case of the *alpha*-halogen acids, by simply heating with water or with alkalis,



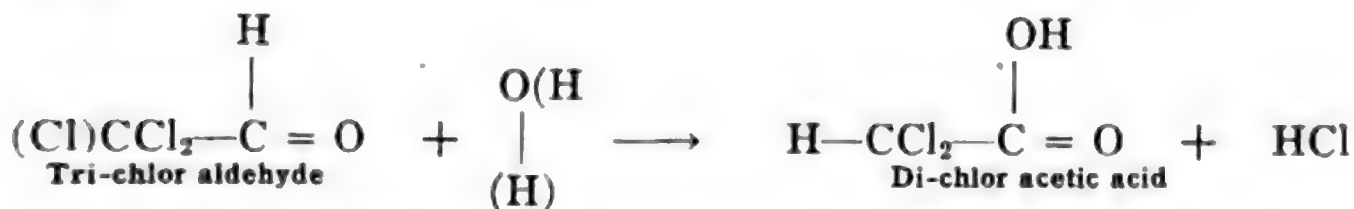
Unsaturated Hydrocarbons.—In the case of *beta*-halogen acids the reaction takes place differently. When these are heated with water and alkali they lose carbon dioxide and the halogen-hydrogen acid, an *unsaturated hydrocarbon* resulting.



The same is true of the *alpha-beta*-di-halogen acids, which, by the loss of halogen-hydrogen acid, yield *halogen unsaturated compounds*.



aldehyde (chloral). The reaction is somewhat complicated and is probably due to the real action of water. It may be represented as follows:



Tri-chlor acetic acid is a solid forming deliquescent crystals which melt at 52° and boil at 195° . It is strongly caustic and is used in medicine on account of this property. It is readily decomposed by boiling its solution, yielding chloroform and carbon dioxide,



This reaction is analogous to the decomposition of saturated acids which, by the loss of carbon dioxide, yield the corresponding hydrocarbon. The halogen acid, however, undergoes the decomposition much more easily than the unsubstituted acid. Though so closely related to both chloroform and chloral, tri-chlor acetic acid does not possess either soporific or anæsthetic properties. If the soporific action of chloral is due to the formation of chloroform in the body, it would seem that tri-chlor acetic acid should also act as a soporific as it decomposes and yields chloroform as easily as does chloral. This is one reason for claiming that the soporific action of chloral is not connected with its decomposition into chloroform. The three chlor acetic acids are of especial importance historically in connection with the development of ideas in regard to substitution as advanced by **Dumas** (p. 9). The fact that acetic acid in which hydrogen (*electro positive*) was substituted by chlorine (*electro negative*), yielding compounds possessing all the properties of the original acetic acid, being even more strongly acid than the acetic acid itself, was in accordance with ideas of **Dumas**, that one element could be substituted for another and act like the one substituted. It was, however, in direct opposition to the *electro-chemical theory* as advanced and upheld by **Berzelius**, for, by this theory, an electro positive element could not be replaced by an electro negative one. The other important halogen acids need not be considered in detail. When they are involved in future discussions they will be mentioned. Neither need we consider, in detail, the halogen unsaturated acids. Enough has been said in regard to the general

properties of these substituted acids, their formation and reactions, to lead us to understand any unsaturated acid of like character. The substituted unsaturated acids bear exactly the same relation to substituted saturated acids that the acids themselves bear to each other and which has been fully discussed in the chapter on unsaturated acids.

II. HYDROXY ACIDS

The hydroxy acids are the most important of all the classes of substituted acids. Many of them occur as constituents of plants or animals and they are closely related to other important natural products such as the sugars. They result from the substitution of the *hydroxyl group*, (—OH), for *hydrogen* of the *alkyl radical* in acids. Being mixed *alcohol and acid* compounds, they possess the properties of *both* classes of compounds represented and these properties are *like* as well as *different*.

As we have not yet studied the *poly-carboxy compounds* our present discussion will include only the *mono-hydroxy* and the *poly-hydroxy* substitution products of the *mono-carboxy acids* (mono-basic acids). The hydroxyl derivatives of the poly-carboxy acids will be considered in connection with these acids when we come to them.

Syntheses.—The general methods for the synthesis of hydroxy acids are numerous, because the reactions that have been used for the preparation of both alcohols and acids are applicable. We have two general types of synthetic reactions.

I. *The introduction of the hydroxyl group, or groups, into mono-carboxy acids.* These reactions will be analogous to those used for the synthesis of alcohols.

II. *The introduction of the carboxyl group, or of some group yielding carboxyl, e.g., the cyanogen group, (—CN), into mono-hydroxy or poly-hydroxy alcohols.* These will be analogous to the reactions used for the synthesis of acids.

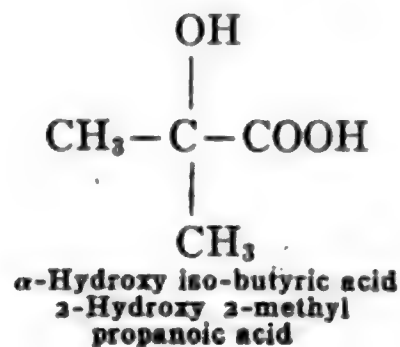
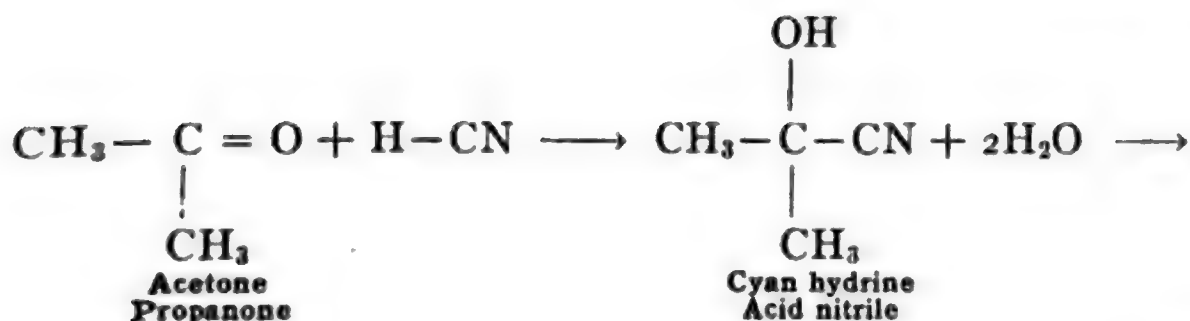
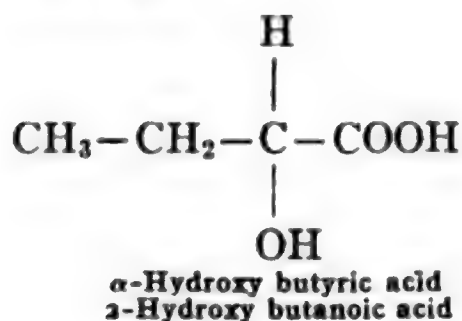
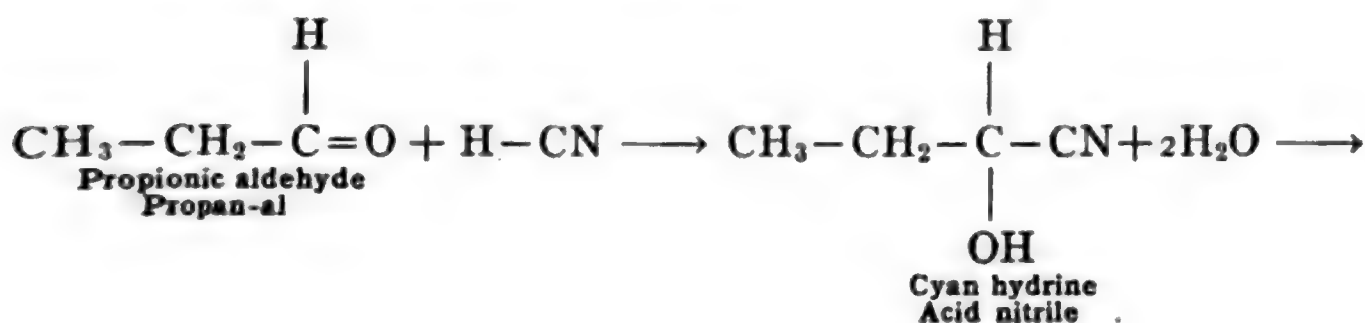
Alcohol-like Syntheses. From Halogen Acids.—The simplest method of synthesizing hydroxy acids, similar to methods for the synthesis of alcohols, is from the corresponding halogen compounds.

1. *Halogen acids* by reaction with water, H—OH , potassium, or sodium hydroxide, K—OH , Na—OH , or silver hydroxide, Ag—OH , yield hydroxy acids by *replacing the halogen with hydroxyl*.



From Amino Acids.—2. *Amino acids*, by diazotization and subsequent decomposition of the resulting diazo compound with water, yield hydroxy acids by the *replacement of the amino group with hydroxyl*. These reactions will be considered when the amino acids are studied.

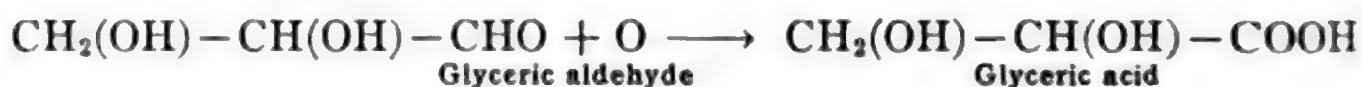
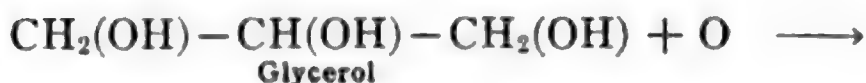
Acid-like Syntheses. From Cyan Hydrines.—3. *Cyan hydrines*, alcohol-cyanogen compounds, when hydrolized yield hydroxy acids by the *conversion of the cyanogen group into the carboxyl group*. As stated under the cyan hydrines (p. 225), and also under aldehydes (p. 116), these alcohol-cyanogen compounds are formed from aldehydes or ketones by the addition of hydrogen cyanide. The double reaction will be, then, as follows:



From *aldehydes*, we always obtain an *alpha*-hydroxy acid in which the hydroxyl group is linked to the carbon atom *which is itself directly linked to carboxyl*. Also the resulting hydroxy acid will always contain *one more carbon* than the aldehyde with which we start. Thus, by starting with any saturated alcohol or acid and obtaining the aldehyde, we may pass to the hydroxy acid next higher in the series. **Acetic aldehyde** yields **α -hydroxy propionic acid**. From *ketones* we also always obtain an *alpha*-hydroxy acid and likewise *increase the number of carbon atoms by one*. The *alpha*-hydroxy acid obtained, however, will be isomeric with the one obtained from the aldehyde of equal carbon content. This will be seen from the above reactions.

The hydroxy acids obtained from aldehydes will contain the group, $-\text{CH}(\text{OH})-\text{COOH}$, and are thus *secondary* alcohols while those obtained from ketones will contain the group, $=\text{C}(\text{OH})-\text{COOH}$, and are *tertiary* alcohols. These reactions are of especial importance in connection with the poly-hydroxy aldehydes and ketones, which, as we shall find, are the sugars. The cyan hydrines, or hydroxy acid nitriles, which are the intermediate products in these reactions, are not isolated as such, the reaction being completed without interruption.

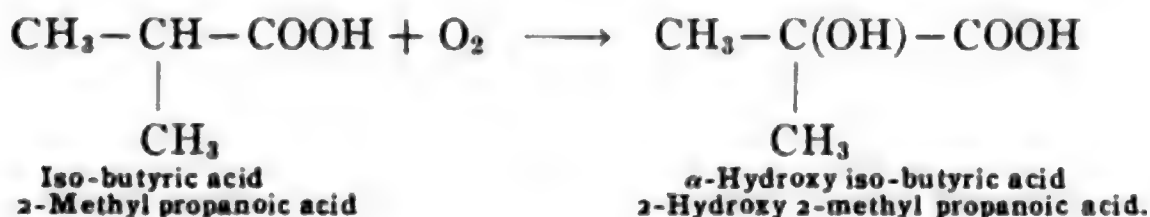
From Poly-hydroxy Alcohols.—4. *Poly-hydroxy alcohols* by oxidation, yield *poly-hydroxy acids*. In this case, of course, only primary alcohol groups, $(-\text{CH}_2\text{OH})$, can yield carboxyl and these groups must, necessarily, be at the end of the carbon chain. The oxidation must be mild so that only one alcoholic group shall be affected.



As the poly-hydroxy aldehydes, or sugars, are the intermediate products in this reaction it is practically the same synthesis if we start with the sugars and oxidize them to the corresponding poly-hydroxy acids.

From Unsubstituted Acids.—5. It will be recalled that hydrocarbons can not be oxidized directly to the formation of alcohols. The reaction which we represent as such (p. 114), is purely hypothetical and is used to show the steps in the complete oxidation of a hydrocarbon in the formation of the successive oxidation products, viz., alcohols, aldehydes and acids. When, however, we have an acid in which there

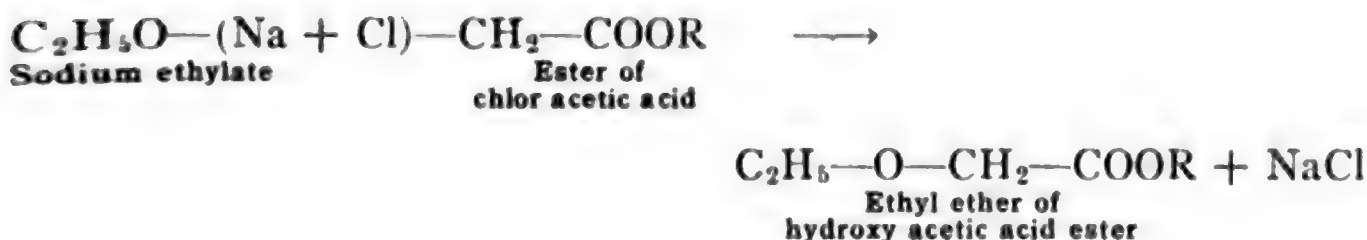
is a *tertiary carbon atom*, e.g., $(R)_2=CH-COOH$, the *tertiary carbon on oxidation has the hydrogen atom oxidized to hydroxyl*, as follows:



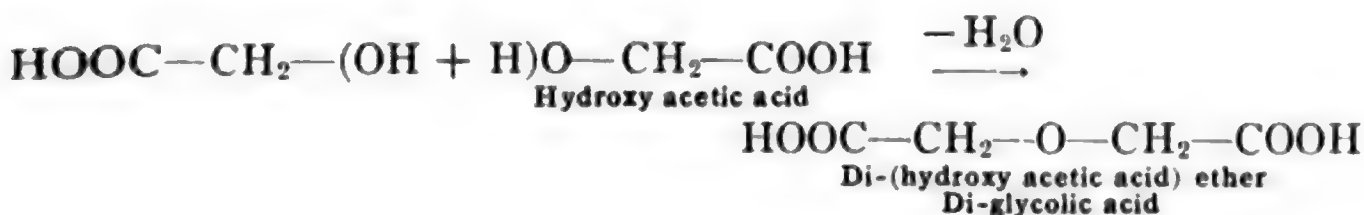
Reactions and Products. Ethers.—Being *both alcohols and acids* the hydroxy acids undergo reactions and yield products characteristic of both classes of compounds. (1) *As acids* they form *metallic salts*, *acid chlorides* and *acid amides*, which are exactly analogous to those formed from the acetic acid series both as to methods of formation and properties. These need not be discussed further. (2) They form *ethers* with other alcohols, in this case reacting *as an alcohol*. These new compounds will be mixed *ether and acid* compounds.



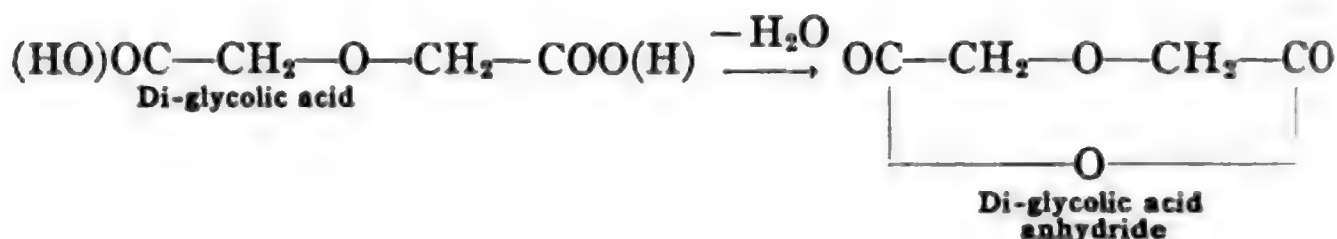
These ethers are usually formed by the reaction of an alcoholate with an ester of a halogen acid, the reaction being analogous to the **Williamson synthesis** of ether.



Not only, however, do the hydroxy acids form ethers with other alcohols but they will react in the same way with themselves, the alcohol group of one molecule forming an ether with the alcohol group of a second molecule.

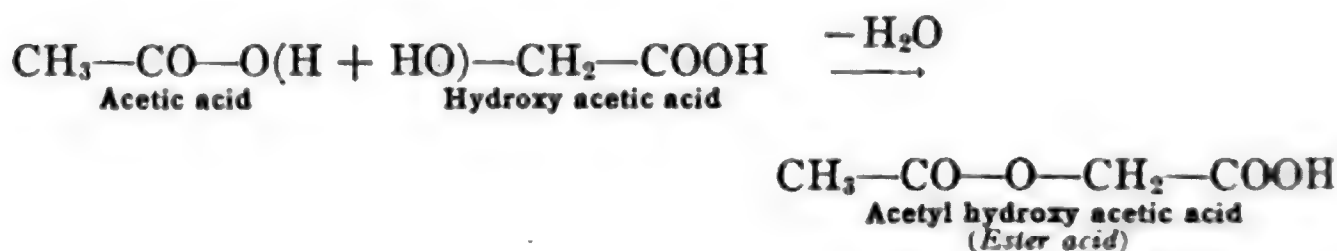


The ether which is obtained in small yields by heating the hydroxy acid is more easily prepared by the reaction between two molecules of chlor acetic acid and potassium hydroxide. As this reaction probably takes place in two steps, the hydroxy acetic acid being first formed from the chlor acetic acid, the formation of the ether may be represented as given. The resulting compound which, in the above case, is an ether of di-(hydroxy acetic acid) is known as **di-glycolic acid**; hydroxy acetic acid itself being **glycolic acid**. It yields an anhydride by the loss of water from the two carboxyls.

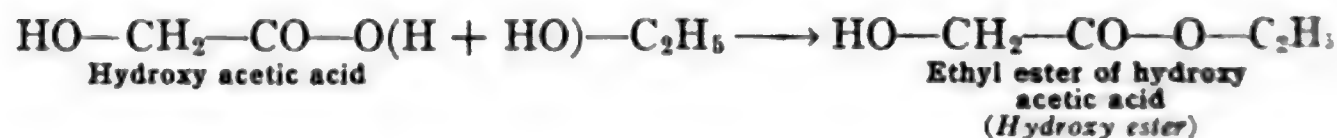


In this anhydride the *open chain* structure of the di-glycolic acid is converted into a *closed ring* structure. This is similar to the *gamma*-anhydrides described below in (7).

Esters with Acids.—(3) The hydroxy acids form *esters with other acids*, in this case also *reacting as an alcohol*. These compounds will be mixed *esters and acids*.

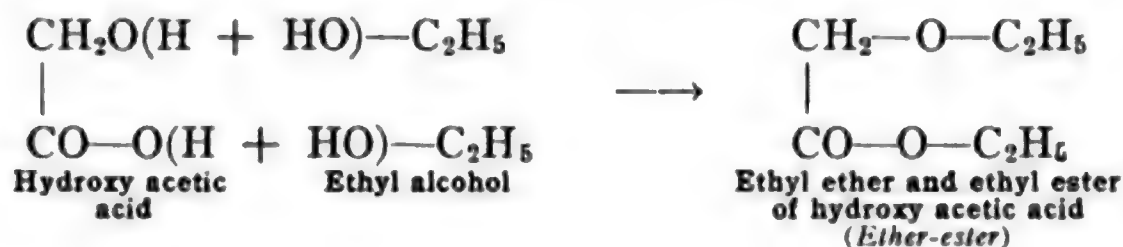


Esters with Alcohols.—(4) They form *esters with other alcohols*, in this case *reacting as an acid*. These compounds are mixed *alcohols and esters* or *hydroxy esters*.

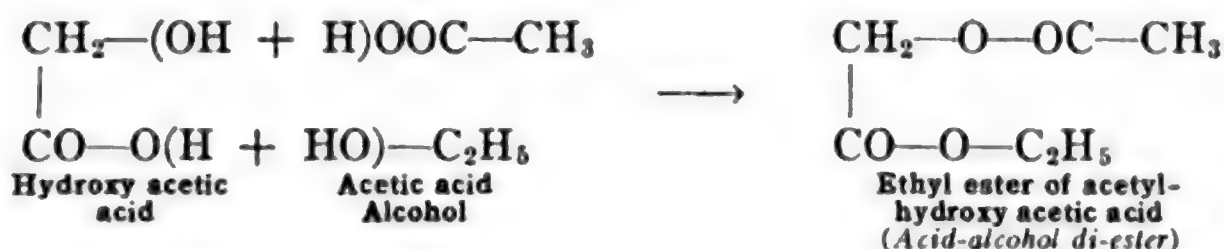


Both reactions (3) and (4) take place also between two molecules of the *alpha*-hydroxy acid itself in which case the product is termed an *anhydride* as discussed below in (7).

Ether-esters.—(5) They form *double ether and ester compounds* in which case they react as both alcohol and acid toward another alcohol.



Mixed Esters.—(6) Still another form of ester would be possible, viz., one in which the hydroxy acid would react as an alcohol to another acid and as an acid to another alcohol. This would give us a *mixed alcohol-acid ester*.

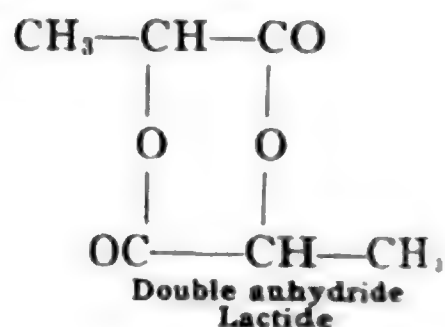
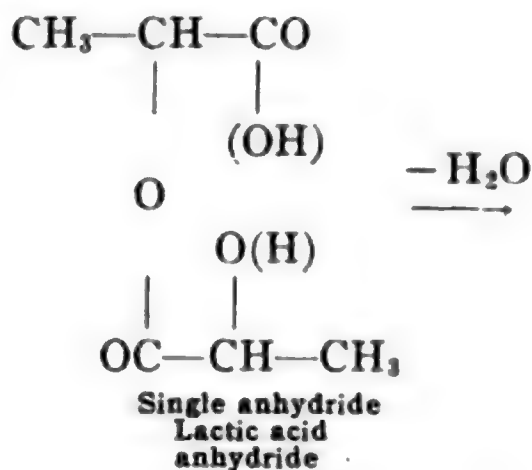
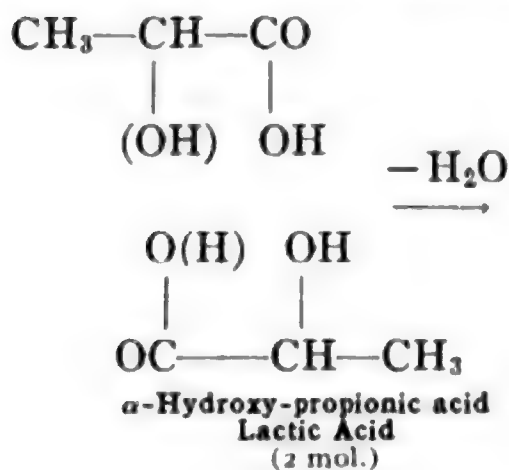


Such a compound is, however, not known. If it were formed it would probably yield an anhydride by two molecules losing two molecules of ethyl acetate. The result would be the same as in the case of *alpha*-hydroxy acid anhydrides as in (7).

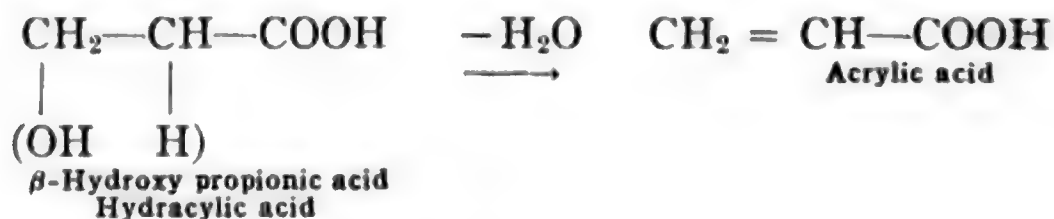
Anhydrides.—(7) The most striking reactions of the hydroxy acids are those in which the *alpha*-, *beta*-, and *gamma*-hydroxy acids react differently. These reactions involve the loss of water and the formation of anhydrides. The reaction takes place simply under the influence of heat, and shows the different effect which is produced by a difference in the position of the hydroxyl group in relation to the carboxyl.

***alpha*-Hydroxy Acid Anhydrides.**—When an *alpha*-hydroxy acid is heated, or when it simply stands over sulphuric acid, two molecules react together as an alcohol-acid compound, in the manner described above in (3) and (4). The *alcoholic hydroxyl of one molecule* reacts with the *acid hydroxyl of the other molecule* and water is lost with the formation of a single anhydride which is really an ester. This compound then loses a second molecule of water by the reaction between the remaining alcoholic and acid hydroxyl groups forming a *double anhydride* or a *double ester* as discussed above in (6). The name of such double anhydride takes the termination *ide* in place of *ic* of the original

acid. In it the open chain structure of the original acid has been converted into a *closed chain* or *ring* structure.



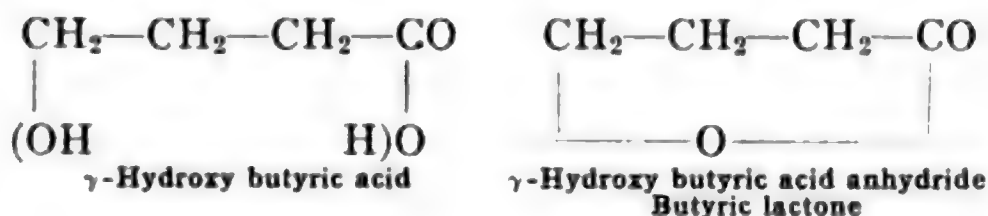
***beta*-Hydroxy Acid Anhydrides.**—When *beta*-hydroxy acids are heated alone, or with potassium hydroxide, water is lost *from one molecule*. In this case *water is formed from the alcoholic hydroxyl and one hydrogen from the neighboring methyl residue*. The product is an *unsaturated acid*. From *beta*-hydroxy propionic acid we obtain **acrylic acid**, as follows:



This reaction is exactly analogous to that taking place with *beta*-halogen acids which by loss of hydrogen halide yield an unsaturated acid (p. 233). In case there are more than three carbon groups the loss of water is almost always between the *alpha*- and the *beta*-carbons.

***gamma*-Hydroxy Acid Anhydrides.**—When solutions of *gamma*-hydroxy acids are heated, often on simply standing at ordinary temperatures, water is lost *from one molecule* and anhydrides result. In the case of the *beta*-hydroxy acids the water is lost from the *alcoholic hydroxyl* and the *hydrogen* of the neighboring carbon group. With the

gamma-hydroxy acids, however, water is lost from the alcoholic and the acid hydroxyl in the same molecule, forming an inner anhydride.

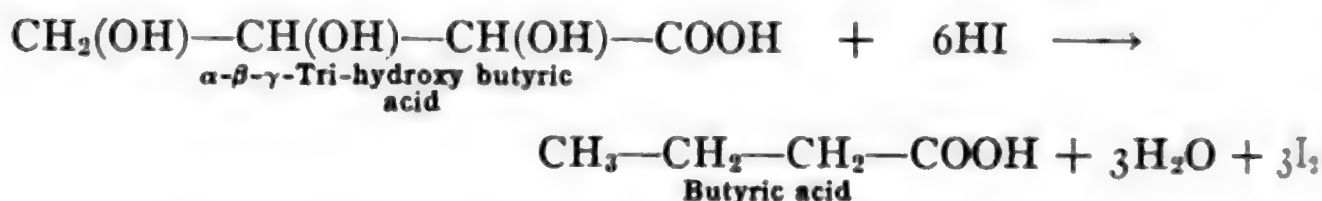


The same reaction takes place with the *delta*-hydroxy acids. The reaction is analogous to that in the case of the *gamma*-halogen acids which, by the loss of hydrogen-halide, form a similar inner anhydride compound. These inner-anhydrides are known by the name of *lactones*, and are distinguished by the letter prefix γ - or δ -, as the case may be. This ready splitting off of water from the two hydroxyl groups in the same molecule will be made clear if the space configuration of the molecule of a *gamma*-hydroxy acid is examined, especially if a model of such an acid be made of tetra-hedral carbon groups. According to the tetra-hedral theory of **van't Hoff**, if four or five carbon groups in a chain have a hydroxyl group on the first and on the fourth or fifth carbon these two hydroxyls will approach very near to each other, in the case of a four carbon compound, and will practically touch each other if five carbons are present.

The above reactions of the hydroxy acids show plainly the variety of products possible because of the mixed alcohol-acid character of the compounds and the readiness with which these two kinds of groups react either with themselves, with each other or with other reagents. We shall find in the study of the amino acids that *alpha*-, *gamma*-, and *delta*-amino acids have this same tendency to form anhydrides. In this case water is lost from the acid hydroxyl and one of the hydrogens of the amino group, the *imino group*, (---NH---), acting as the uniting link, like the oxygen in the above cases. The conversion of *gamma*- or *delta*-hydroxy acid or amino acid *open chain* compounds into *closed ring* or *cyclic* compounds is of great significance in connection with the relation between the two classes of compounds.

Reduction.—(8) When hydroxy acids are treated with hydrogen iodide they are readily reduced to the unsubstituted acid. In other words, the hydroxyl group is reduced to hydrogen. In this reaction the hydroxyl group is first replaced by iodine giving the iodine substituted acid. This is then reduced because of the strong reducing

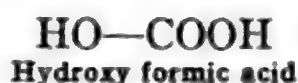
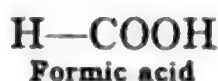
power of hydrogen iodide. With hydrogen bromide, which is not so strong a reducing agent, the reaction stops with the halogen substituted acid. The reaction takes place especially with the poly-hydroxy acids.



This is an important reaction for *converting the poly-hydroxy acids into simpler acids*.

Hydroxy Formic Acid $\text{HO}-\text{COOH}$

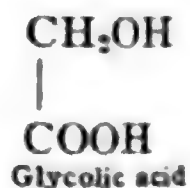
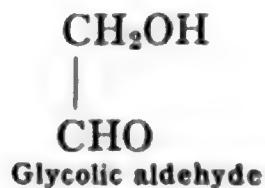
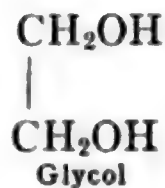
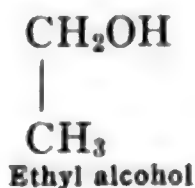
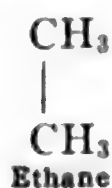
While **hydroxy formic acid** is the simplest of the hydroxy mono-carboxy acids it will not be discussed here because, as may be seen if the formula is examined, it corresponds to the hypothetical **carbonic acid**, H_2CO_3 .



As hydroxy formic acid is undoubtedly identical with carbonic acid it will be studied later as the latter compound (p. 425).

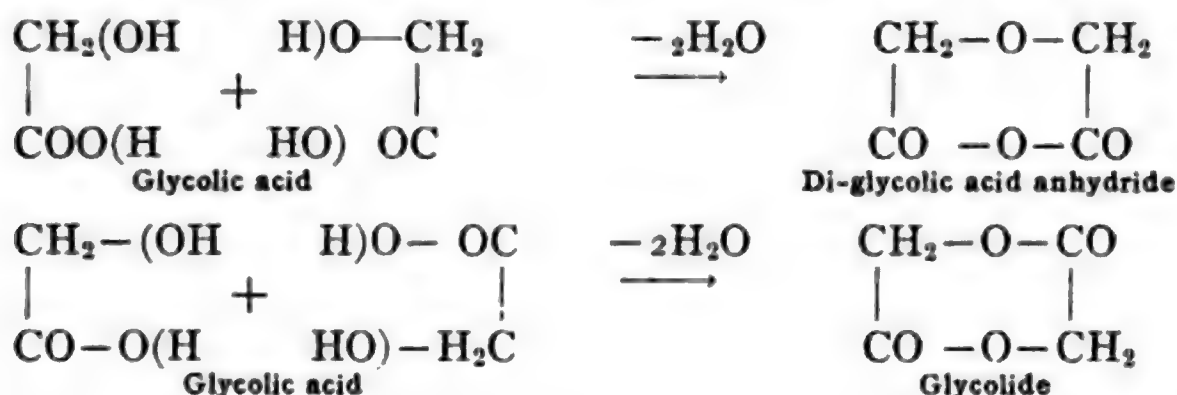
Hydroxy Acetic Acid $\text{CH}_2(\text{OH})-\text{COOH}$

The next higher hydroxy acid is **hydroxy acetic acid** $\text{CH}_2(\text{OH})-\text{COOH}$, known also as **glycolic acid**. It may be prepared (a) *from chlor acetic acid*, (b) from the *cyan-hydrine* obtained from **formic aldehyde**, or (c) *by the oxidation of ethylene glycol*, by reactions which have been already discussed. Its relation to ethylene glycol gives it the name of glycolic acid. It may be considered as a direct oxidation product of ethane.



Glycolic acid is a crystalline solid melting at $79^\circ-80^\circ$, and is easily soluble in water. It forms an anhydride, ethers and esters as has been explained for hydroxy acids in general. As there are only two carbon atoms present no other hydroxy acetic acid is possible. The *double anhydride* of glycolic acid is known as **glycolide** and is obtained when

glycolic acid is heated. It is isomeric with **di-glycolic acid anhydride** (p. 240). The difference in these two isomers is plainly shown in their structural formulas and in their formation from glycolic acid.

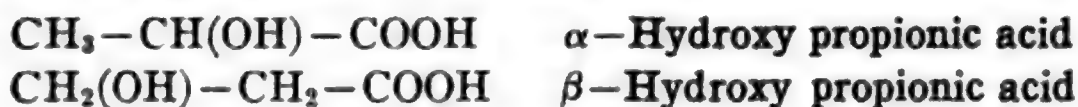


Both are obtained from *two molecules of glycolic acid by the loss of two molecules of water*. In **di-glycolic acid anhydride** one molecule of water is formed from the two alcohol hydroxyls and one from the two acid hydroxyls. In **glycolide** each molecule of water is formed from one alcohol hydroxyl and one acid hydroxyl. The first is an *anhydride* of an ether-acid, di-glycolic acid, while glycolide is a *double ester* of an alcohol-acid.

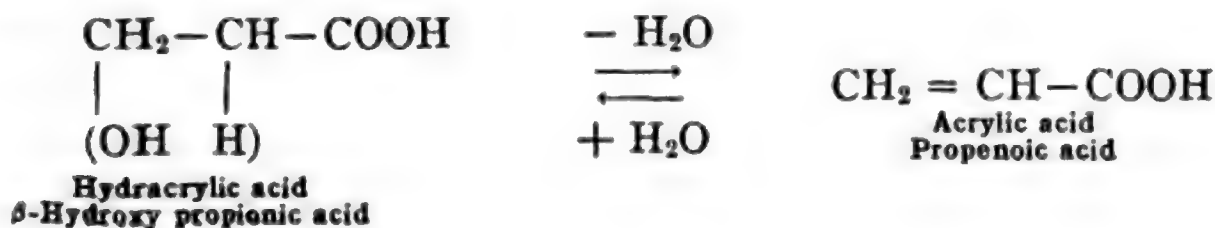
Hydroxy Propionic Acids

Hydracrylic acid $\text{CH}_2\text{OH}-\text{CH}_2-\text{COOH}$ **β -Hydroxy propionic acid**

Propionic acid plainly yields two isomeric hydroxy acids, viz., an *alpha*- and a *beta*-acid. The constitution of the two compounds is,



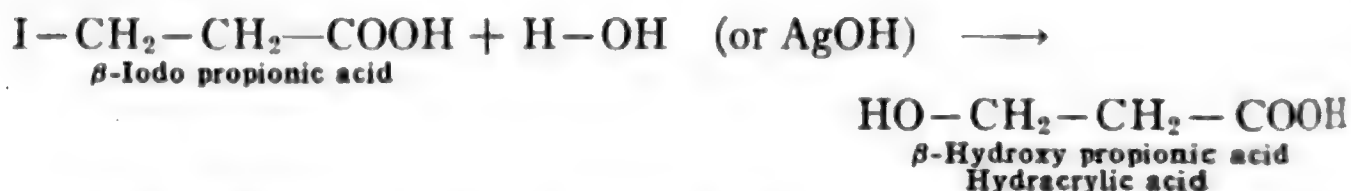
We have just spoken of the different action of the *alpha*-, *beta*-, and *gamma*-halogen acids toward alkalis (p. 233), and of the similar different action of the *alpha*-, *beta*-, and *gamma*-hydroxy acids when dehydrated (p. 241). The second of the above acids, viz., the **β -hydroxy propionic acid**, shows the reaction characteristic of *beta*-acids. On heating, or by the action of sulphuric acid, it loses water and is converted into the corresponding ethylene unsaturated acid, **propenoic acid**, as follows:



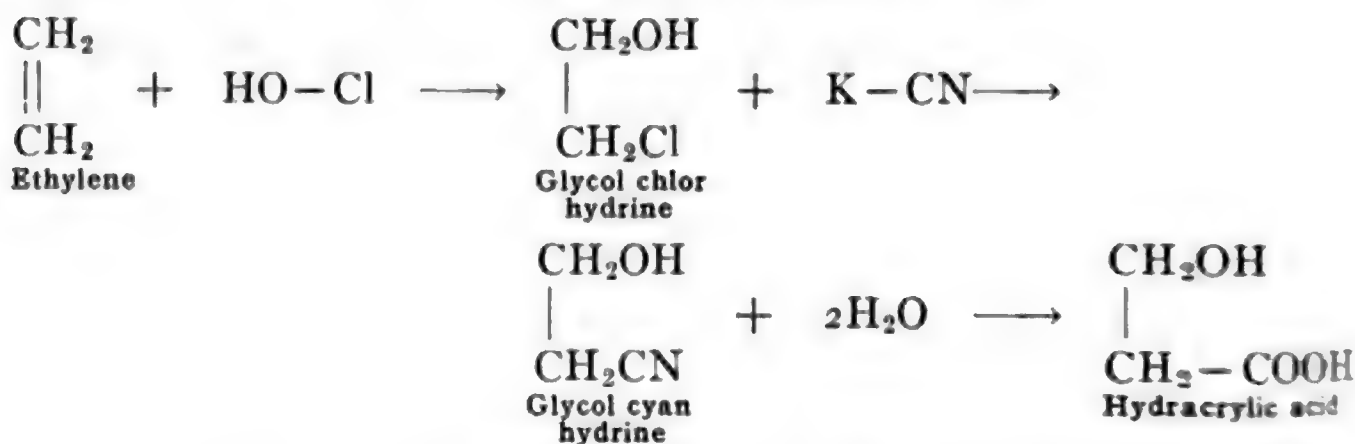
Propenoic acid is commonly known as **acrylic acid** (p. 172), and **β -hydroxy propionic acid** is therefore named **hydracrylic acid**, i.e., hydrated acrylic acid.

Synthesis from Acrylic Acid.—Three methods of synthesis of hydracrylic acid show its relation to acrylic acid, to propionic acid and to ethylene. When acrylic acid is heated with sodium hydroxide to 100° it takes up a molecule of water and yields hydracrylic acid. The reaction is simply the reverse of the one above.

From Propionic Acid.—The simplest method of synthesis is the one which shows the relation of hydracrylic acid to propionic acid and proves that it is the *beta*-hydroxy acid. When **β -iodo propionic acid** is boiled with water, or with aqueous silver hydroxide, hydracrylic acid is obtained.



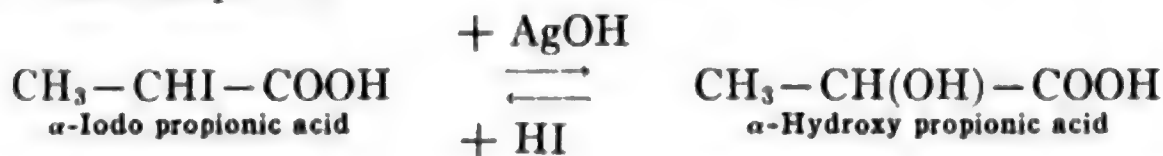
From Ethylene.—The reverse of this reaction takes place when hydracrylic acid is treated with hydrogen iodide, HI, as discussed above in (8). The third synthesis of hydracrylic acid shows its relation to ethylene. Ethylene takes up, by addition, hypochlorous acid, HO—Cl, in just the same way as it does bromine or hydrobromic acid. The compound obtained is **glycol chlor hydrine**. This chlor hydrine, by treatment with potassium cyanide, is converted into the **glycol cyan hydrine**. The cyan hydrine, being an acid nitrile, yields an acid on hydrolysis. The acid obtained is **hydracrylic acid**.



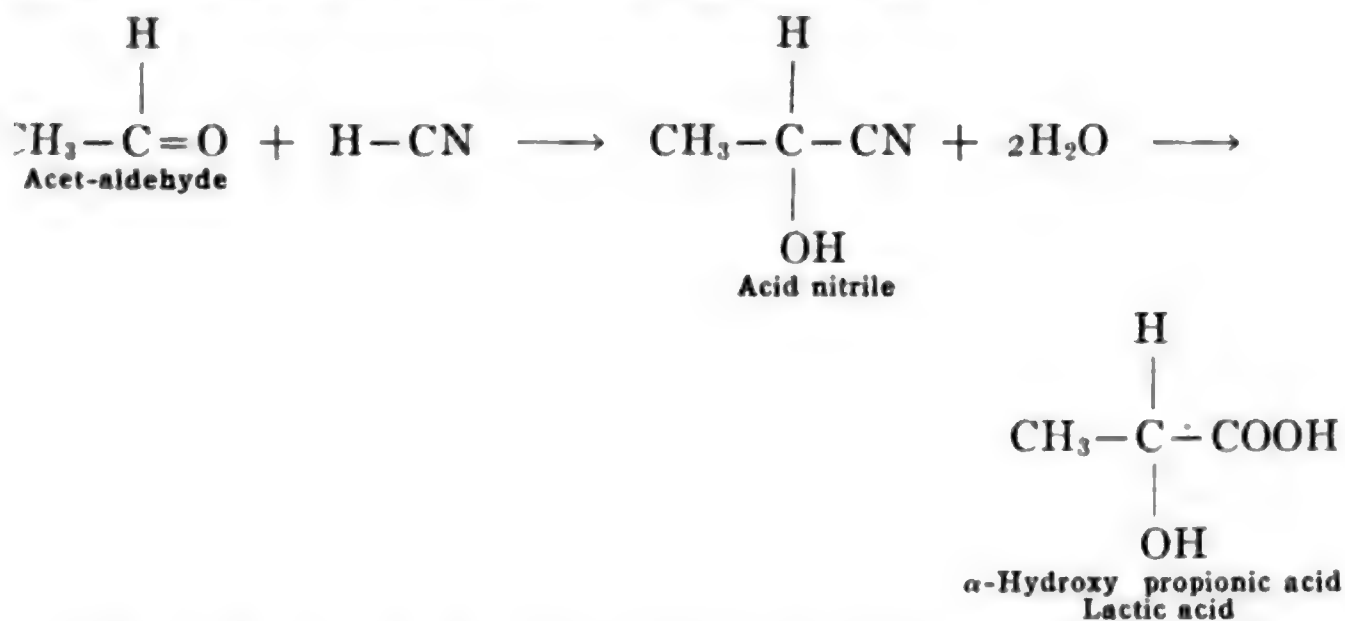
Lactic Acid $\text{CH}_3-\text{CH}(\text{OH})-\text{COOH}$ **α -Hydroxy Propionic Acid**

The isomeric *alpha*-hydroxy acid is prepared from **α -iodo propionic acid** in exactly the same way as the *beta*-acid is prepared from the *beta*-

iodo compound. The reverse reaction, viz., the conversion of the *alpha*-hydroxy acid into the *alpha*-iodo acid, also takes place though in this case action goes further and the unsubstituted propionic acid is obtained as in (8) above. Both of these reactions prove the constitution of the compound.

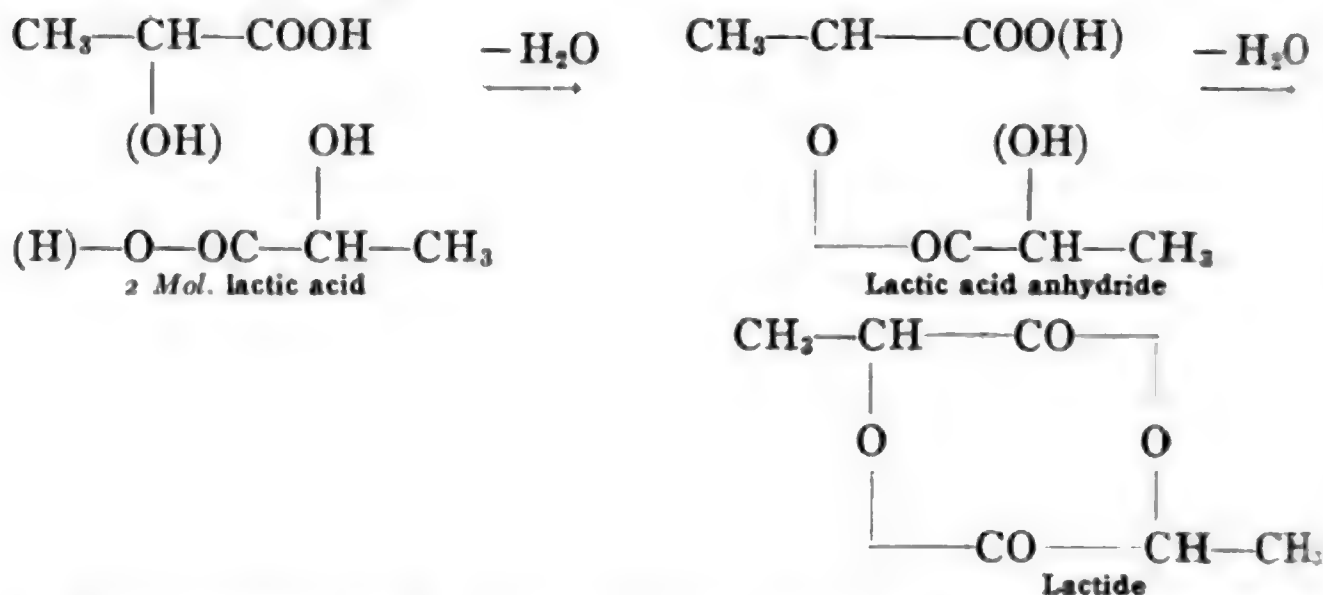


The synthesis from acet-aldehyde also proves this constitution. By the addition of hydrogen cyanide acet-aldehyde yields a cyan hydrine in which the hydroxyl and cyanogen groups are linked to the same carbon. This cyan hydrine, like glycol cyan hydrine, being an acid nitrile, yields an acid on hydrolysis. The acid, so obtained is **actic acid** which therefore must be an *alpha*-hydroxy acid containing three carbon atoms, i.e., ***alpha*-hydroxy propionic acid**.



This *alpha*-acid is of much greater importance than the isomeric *beta*-acid, **hydracrylic acid**. It is commonly known as **lactic acid** and occurs in nature, being present in *sour milk* where it is produced by the acid fermentation of milk-sugar due to bacterial action. Considering both the carboxyl and hydroxyl as substituting groups these two acids may be considered as *di-substituted ethanes*. As such the *beta*-acid has the ethylene or *symmetrical* structure and the *alpha*-acid has the ethylidene or *unsymmetrical* structure. On this account the former is sometimes called **ethylene lactic acid** and the latter, **ethylidene lactic acid**. The names are not, however, good as the *beta*-acid, **hydracrylic acid**, is in no sense a lactic acid.

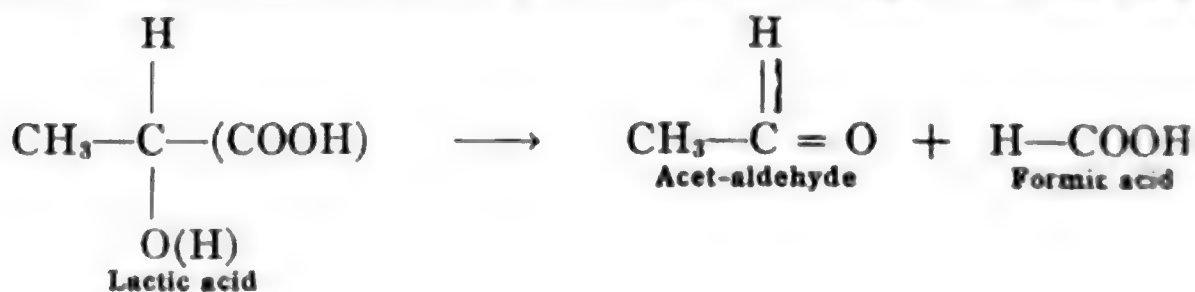
Reactions. Anhydrides.—The most important reaction of lactic acid is its formation of anhydrides. As explained previously (p. 241) for *alpha*-hydroxy acids in general, the anhydrides formed are two. The first, known as **lactic acid anhydride**, is formed by the loss of *one* molecule of water from two molecules of the acid. The second is a closed ring compound, or *inner anhydride*, and is known as **lactide**, being analogous to **glycolide**. It is formed by the loss of *two* molecules of water from two molecules of the acid or by the loss of one more molecule of water from the single anhydride. Lactic acid anhydride, the first compound, is produced by heating the acid to 130° – 140° , or even at ordinary temperatures in dry air. It is an easily soluble amorphous compound. The lactide is obtained by passing dry air through lactic acid heated to 150° . It is an almost insoluble crystalline substance melting at 255° .



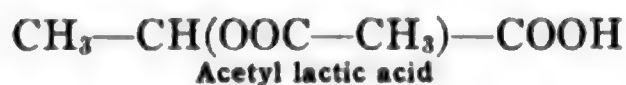
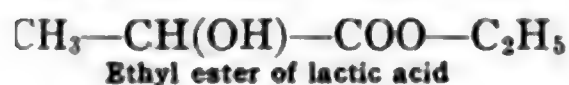
Pyro-racemic Acid.—By oxidation lactic acid has the secondary alcohol group converted into a carbonyl group yielding a *ketone acid* known as **pyro-racemic acid** (p. 253).



When heated with dilute sulphuric acid lactic acid is split into acet-aldehyde and formic acid. The reaction resembles the reverse of the reaction of its formation from acet-aldehyde through the cyan hydrine.



By bacterial fermentation the calcium salt of lactic acid is decomposed into salts of simpler acids, *e.g.*, **propionic**, **butyric** and **valeric**. As an acid lactic acid yields an *ethyl ester* with ethyl alcohol and as an alcohol it yields, with acetic anhydride, an *acetyl derivative*. The latter compound results from the putrefaction of muscular tissue, as this contains both lactic and acetic acid.



Stereo-isomerism.—In addition, however, to the two structurally isomeric acids which we have been considering, one being an *alpha*-hydroxy acid, the other a *beta*-hydroxy acid, there are known two other acids of the same composition both of which prove to be **α -hydroxy propionic acid**. Of these three *alpha*-acids two are *optically active*, one being *dextro*- and the other *levo*-rotatory. The third is optically *inactive* but resolvable into its optical components. An examination of the formula of α -hydroxy propionic acid shows that it contains an asymmetric carbon atom.

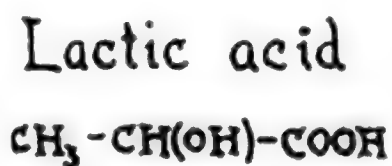
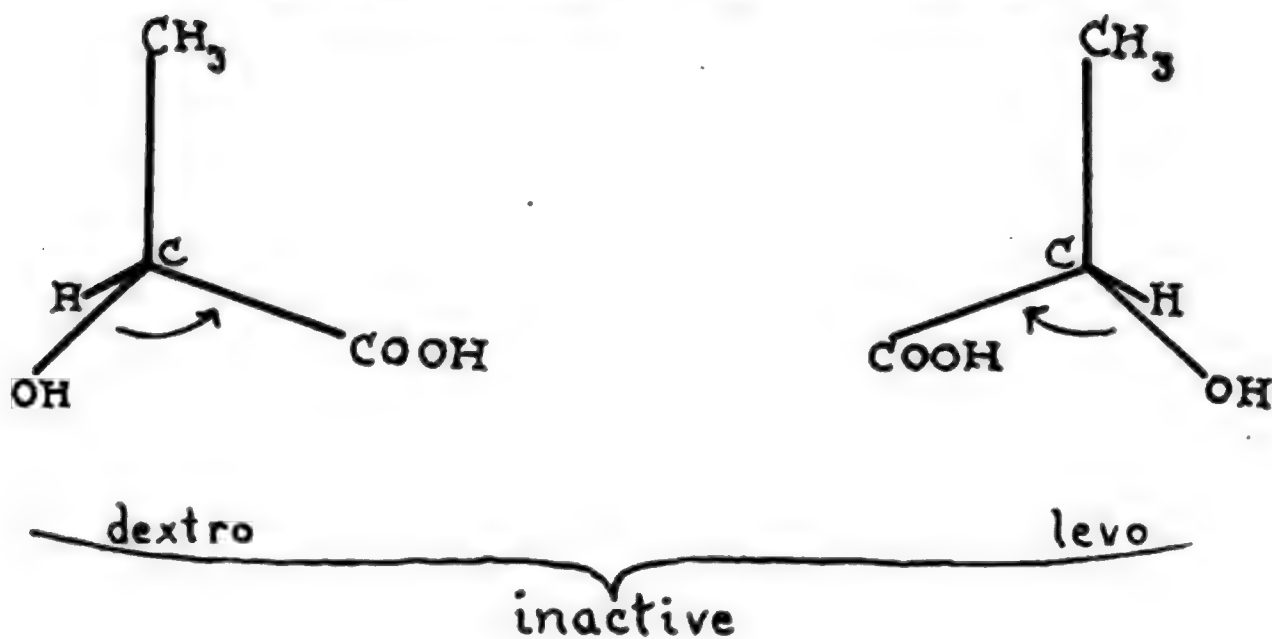
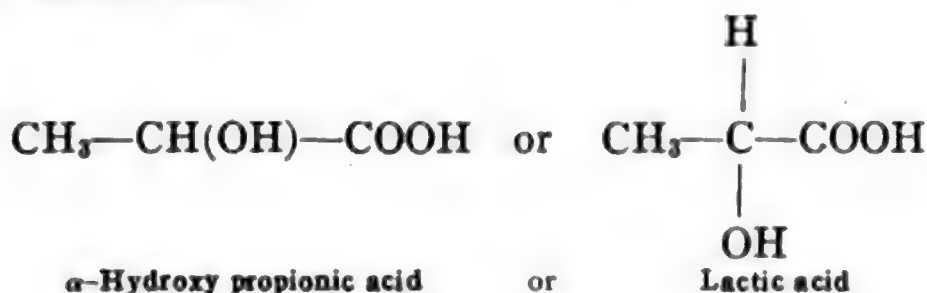


FIG. 4.

The existence of three stereo-isomeric lactic acids is therefore explained in exactly the same way as the three stereo-isomers in the case of **active amyl alcohol**, **2-methyl butanol-1** (p. 90). We need not repeat the discussion of stereo-isomerism as explained by the **van't Hoff-LeBel** theory of the asymmetric carbon atom, *i.e.*, the tetra-hedral theory. The discussion as previously given for the amyl alcohols, applies exactly in the present case.

Inactive or Fermentation Lactic Acid.—**Lactic acid** was discovered by **Scheele**, in sour milk, in 1780. The souring of milk is caused by this formation of lactic acid, producing the result known as *curdling* which is the coagulation of the milk protein **casein**. The lactic acid is formed by the *bacterial fermentation* of the **milk sugar** present in the milk and the stereo-isomeric variety thus formed is the one that is optically *inactive*. **Inactive lactic acid** is thus also known as **lactic acid of fermentation** or simply as ordinary lactic acid. It may also be produced by the action of certain bacteria upon **glucose** or upon **cane sugar** and by the action of alkalies upon substances containing sugar, especially if considerable invert sugar is present, as in the case of molasses. Commercially lactic acid is made from the *whey* of milk left after the cheese curd has been removed. This whey contains all of the milk sugar of the milk. Also the molasses left after the greater part of the milk sugar has been crystallized out is used. Other commercial sources of lactic acid are cane sugar and glucose sugar that has been made by the hydrolysis of starch. In all of these cases in which sugar is fermented lactic acid bacteria are added in the form of sour milk, putrid cheese or pure cultures. Ordinary lactic acid is a colorless thick liquid boiling at 120° , (12 mm.), and with a specific gravity of 1.248. It is difficult to obtain it pure as it always contains more or less anhydride. The purest usually obtained is about 80 per cent and has a specific gravity of 1.21. The chief uses of lactic acid are in medicine, in the form of salts, and in dyeing and tanning. The most common salts are the calcium, zinc and iron lactates. Like other inactive asymmetric compounds inactive lactic acid may be split into its optical components, *i.e.*, the dextro and the levo lactic acids. The strychnine salt is the salt used for this splitting.

Dextro Lactic Acid or Sarco-lactic Acid.—**Dextro lactic acid** is found in muscular tissue and on this account it is known as **sarco-lactic acid**. It is also known as para-lactic acid. It was discovered by **Liebig**

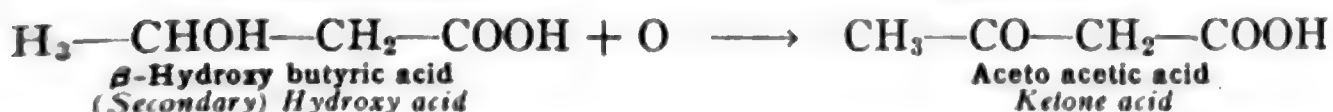
in the juices of flesh and is present in meat extracts. It is found normally in *blood* and in *urine*. It is also produced by the fermentation of the sugars previously mentioned by the action of specific bacteria. It resembles the inactive lactic acid in all of its properties except its optical activity. It forms anhydrides less easily than the inactive acid. Its zinc salt is more soluble and its calcium salt less soluble than the same salts of the inactive acid. An interesting fact is that the salts of *dextro* lactic acid are *levo* rotatory. The anhydride is also *levo* rotatory and by heating is converted into the anhydride of the inactive lactic acid.

Levo Lactic Acid.—**Levo lactic acid** was first obtained by the fermentation of cane sugar by specific bacteria. It is *levo* rotatory but, like the *dextro* acid, the rotation of its salts and its anhydride is reversed, being *dextro* rotatory. The *levo* lactic acid and also the *dextro* acid may be obtained by splitting the inactive acid into its optical components by means of its strychnine salt.

In addition to being present in sour milk lactic acid is found in *ensilage*, in *sauer-kraut* and in various liquids and tissues of the human body, *e.g.*, gastric juice, the fermented juice of muscle, the brain, the blood and the urine. In most of its occurrences in the human body it is the *dextro* lactic acid which is present. In these cases it is probably the result of the fermentation of sugars. The occurrence of lactic acid in the human body is of great physiological importance. It has been found that it is connected with muscular and nervous fatigue and with the oxidation of glucose in the cells. In connection with its formation by the fermentation of sugars it is probable that it is an intermediate product in the alcoholic fermentation of sugars.

III. ALDEHYDE ACIDS AND KETONE ACIDS

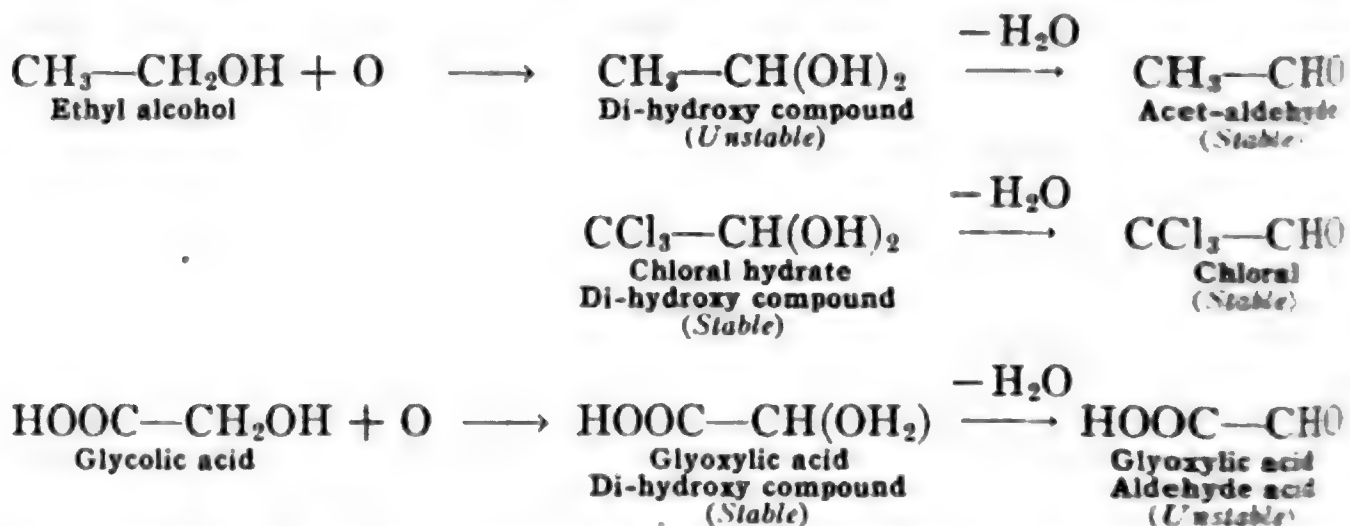
This group of mixed substitution products embracing compounds that are *both aldehyde or ketone and acid* in character are directly related to the mixed alcohol and acid compounds. If a hydroxy acid containing a primary alcohol group has this group oxidized the first product will be an *aldehyde acid*. Similarly if the alcohol group is a secondary one the oxidation product will be a ketone acid.



ALDEHYDE ACIDS

Glyoxylic Acid $\text{CH(OH)}_2\text{—COOH}$ or CHO—COOH

This acid may be prepared by the oxidation of **glycolic acid** as above but better from **di-brom acetic acid** by the action of water. These reactions are analogous to the preparation of acetic aldehyde by the oxidation of ethyl alcohol and by the action of water upon unsymmetrical di-brom ethane (p. 115). In both of these latter cases the reaction has been represented as taking place with the formation of an unstable intermediate product containing two hydroxyl groups linked to one carbon atom which by loss of water yields the aldehyde. In glyoxylic acid, however, we have evidence that this intermediate product is the stable compound, for the composition of it corresponds to the formula $\text{HOOC—CHO.H}_2\text{O}$ or HOOC—CH(OH)_2 . It is impossible to drive off this extra H_2O without decomposing the compound. It will be recalled also that in chloral hydrate we have the same facts in regard to the composition of this compound though in this case the water may be driven off leaving a stable compound, chloral. Placing these three compounds, viz., **acet-aldehyde**, **chloral hydrate** and **glyoxylic acid**, together we can see the similarity and relation.



Now in both glyoxylic acid and chloral hydrate the carbon atom holding the two hydroxyl groups is linked to a *strongly negative carbon group*, viz., $(\text{CCl}_3\text{—})$ or (—COOH) , and it is thought that this condition *gives stability to the two hydroxyl groups linked to one carbon atom*. We shall find later (p. 297) in the case of **mesoxalic acid** that the same condition exists. We may say, therefore, that while the evidence is not absolutely conclusive yet it indicates that in glyoxylic acid we have a di-hydroxy compound in accordance with its composition and the composition of its

Formyl Acetic Acid $\text{H}-\text{CO}-\text{CH}_2-\text{COOH}$

Glucuronic Acid or Glycuronic Acid $\text{CHO}-(\text{CHOH})_4-\text{COOH}$

KETONE ACIDS

Pyro-racemic Acid $\text{CH}_3\text{—CO—COOH}$. **Pyruvic Acid**

$$\text{CH}_3\text{CO}(\text{Cl} + \text{Ag})\text{CN} \longrightarrow \text{AgCl} + \text{CH}_3\text{CO}\text{CN} + 2\text{H}_2\text{O}$$

Acetyl chloride **Acetyl cyanide**


$$\text{CH}_3\text{—CBr}_2\text{—COOH} + \text{AgO} \longrightarrow \text{CH}_3\text{—CO—COOH} + 2\text{AgBr}$$

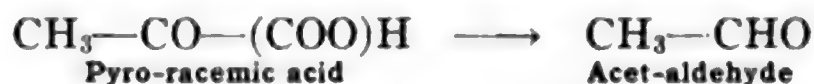
α - α -Di-brom propionic acid Pyro-racemic acid

From Lactic Acid.—When lactic acid, α -hydroxy propionic acid, is oxidized pyro-racemic acid is obtained as was recently stated (p. 248). Also pyro-racemic acid may be reduced to lactic acid.



Physiologically pyruvic acid is associated with lactic acid and glucose in the oxidation of the latter in the cells.

From Acetic and Formic Acids.—A fourth method of synthesis from acetic and formic acid esters will be explained in detail in connection with the next acid. All of these syntheses prove the constitution of pyro-racemic acid as an *alpha*-ketone acid as given. It may be considered as **aceto formic acid** which is in accord with the fourth method of synthesis. As an acid it forms all acid derivatives and as a ketone it undergoes the characteristic ketone reactions, *e.g.*, with phenyl hydrazine and hydroxyl amine. On heating to 150° with dilute sulphuric acid in a sealed tube it loses carbon dioxide and yields acet aldehyde.

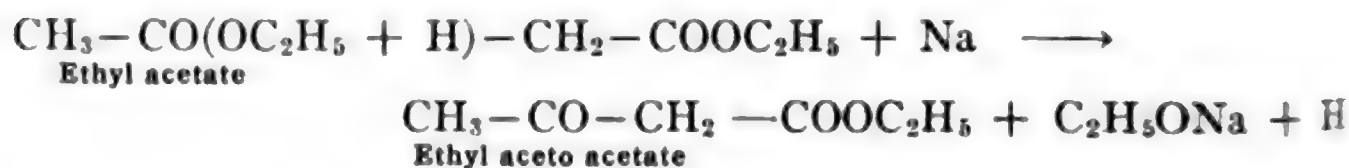


This reaction is analogous to the formation of methane from acetic acid (p. 7).



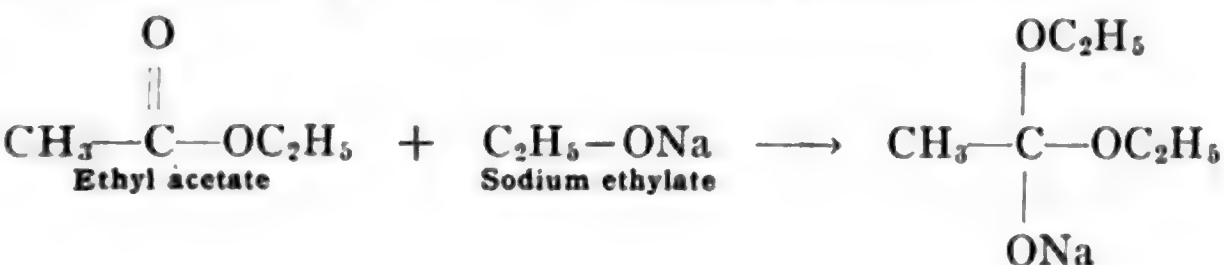
This corresponds to pyro-racemic acid in being the simplest *beta*-ketone acid possible. While it is known in the free state as an easily decomposed hygroscopic syrup its principal form is as the *ethyl ester*, $\text{CH}_3\text{—CO—CH}_2\text{—COOC}_2\text{H}_5$, **ethyl aceto acetate**. In this form it is prepared and in this form it is used as a synthetic reagent. The ester is a colorless liquid boiling at 181° , with a characteristic fruity odor.

Preparation of Ethyl Aceto Acetate.—Ethyl aceto acetate is made by the action of metallic sodium upon ethyl acetate. The reaction may be represented in its simplest form as follows:

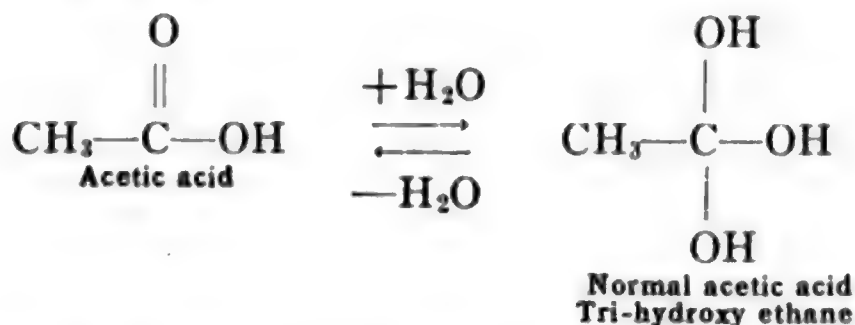


While this reaction represents truly the beginning and end products it has been shown by Claisen and others that it takes place in several steps

and that the presence of **sodium ethylate** is essential. A little alcohol present in the ethyl acetate reacts with the sodium forming sodium ethylate, but if the ethyl acetate has been purified so that it is free from alcohol then the reaction does not proceed except at higher temperatures and then very slowly. The sodium ethylate reacts with the ethyl acetate forming an addition product which is a mixed sodium salt and ethyl ester of normal or tri-hydroxy acetic acid.

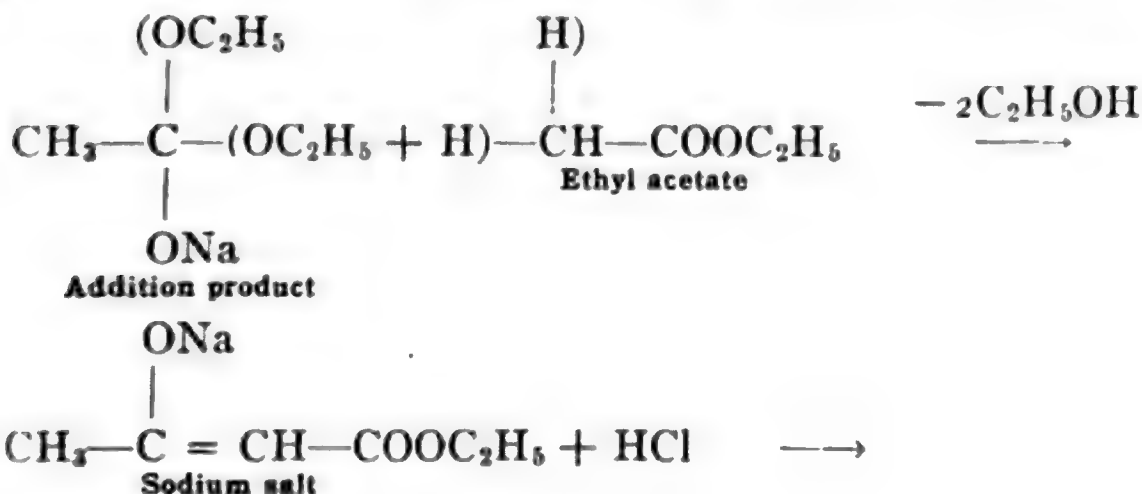


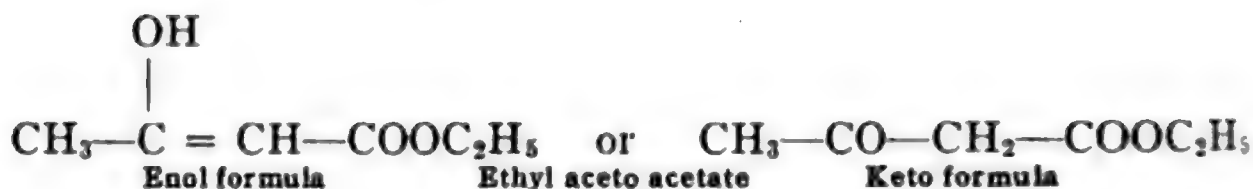
This is analogous to the relation between acids and the so-called normal acids and gives support to the idea that normal carboxy acids are tri-hydroxy compounds.



This addition product formed from ethyl acetate and sodium ethylate now reacts with a second molecule of ethyl acetate losing two molecules of ethyl alcohol and forming the sodium salt of ethyl aceto acetate which on acidifying yields the free ester.

The ethyl alcohol formed as the other product reacts with sodium yielding more sodium ethylate and the reaction continues.



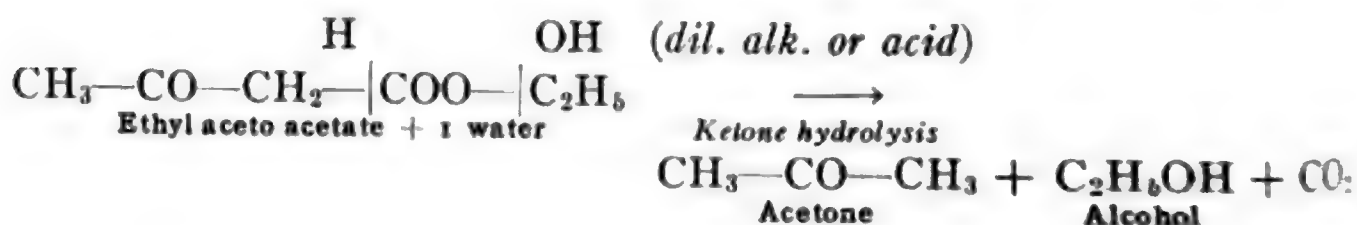


This reaction, however, yields a compound containing a *hydroxyl* group instead of a *carbonyl* group and the question is which is the true formula and which represents the constitution of aceto acetic ester? The answer, strange as it may seem, is that both are right for we have reactions some of which prove one and some the other constitution.

Tautomerism.—This brings us to the discussion of a new phenomenon known as *tautomerism* which, though similar to *isomerism*, is yet distinct from it. In the case we are discussing the two formulas do not represent *different* compounds but the *same* compound. Under certain conditions with certain reagents one constitution holds true, while under other conditions and with other reagents, the other formula represents the constitution. The fact has been well demonstrated by physical chemical study that both forms exist at the same time in equilibrium. This condition of equilibrium varies and may be affected by reagents so that by changing the conditions or the reagents the amount of either form may be increased or diminished, the compound reacting as though it was of one form only. This, then, is what is termed *tautomerism* and the two forms are known as *tautomeric forms*.

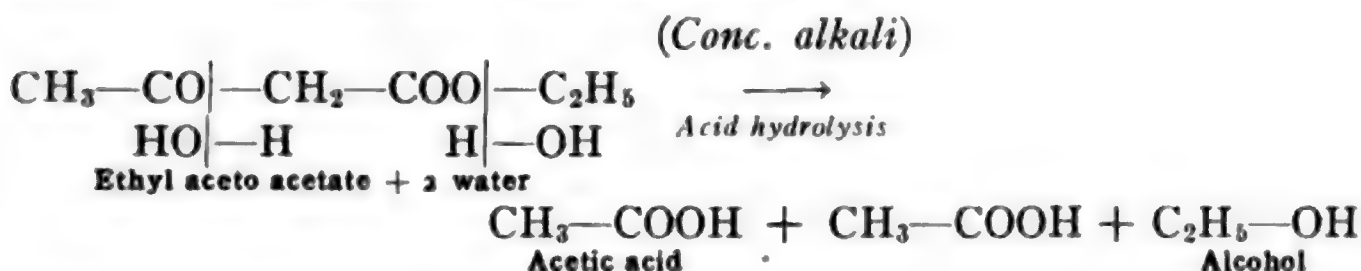
Enol and Keto.—The formula containing the hydroxyl group is termed the *enol* form while the one with the carbonyl group is known as the *keto* form.

Ketone Hydrolysis.—The reactions of ethyl aceto acetate are important and lead to the extensive use of the compound as a synthetic reagent. With water in the presence of alkali or acid two distinctly different hydrolyses take place. When boiled with dilute alkali or dilute acid hydrolysis with loss of carbon dioxide occurs as follows:



The product is acetone, a ketone, and this decomposition is known as the *ketone hydrolysis*.

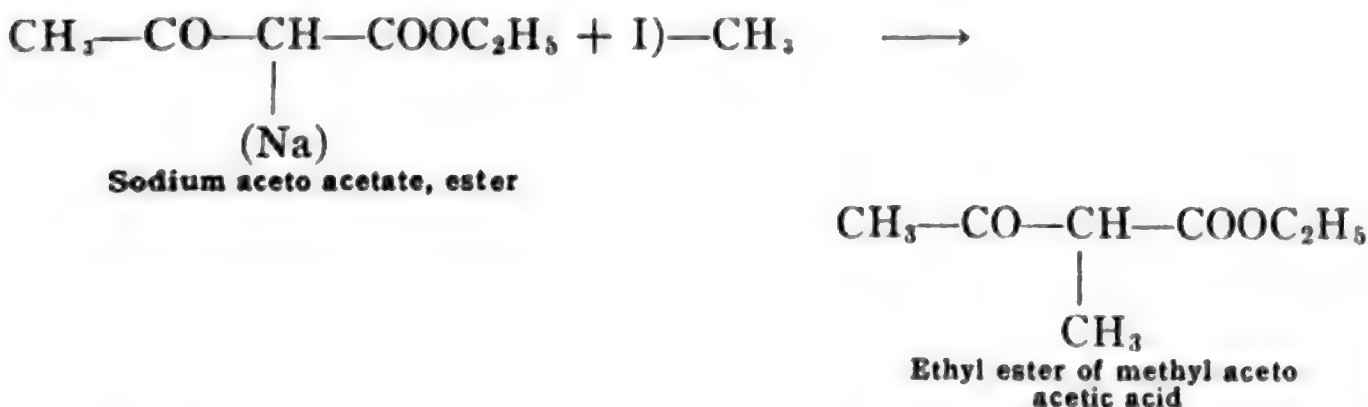
Acid Hydrolysis.—When concentrated alkali or alcoholic alkali is used the hydrolysis takes place differently.



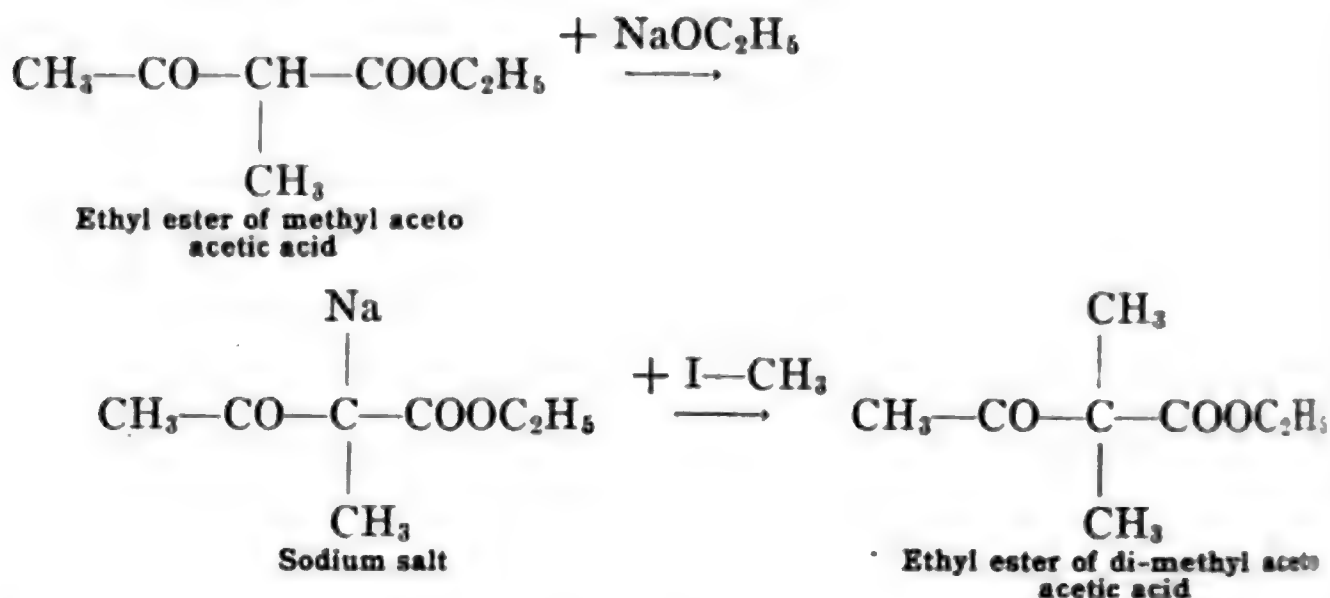
The product here is an *acid* and the reaction is termed the *acid hydrolysis*. Both of these hydrolyses are more easily explained by the *keto* constitution for the ethyl aceto acetate.

Sodium Salt.—The most characteristic reactions of the compound are the formation of a sodium salt and the subsequent reactions of this salt. In the synthesis from ethyl acetate and sodium (sodium ethylate) the sodium salt is the form in which the compound is obtained prior to acidifying. The sodium salt may also be prepared from the free ester by treating with sodium ethylate. The formation of such a metal salt in which the sodium has replaced a hydrogen atom seems to indicate the presence of a *hydroxyl* group. This supports the hydroxy or *enol* form, the salt being $\text{CH}_3\text{—C(ONa) = CH—COOC}_2\text{H}_5$. The reactions of this salt, however, seem to indicate the *keto* form as the true constitution. The formula for the salt in this form is $\text{CH}_3\text{—CO—CHNa—COOC}_2\text{H}_5$. Such replacement of a hydrogen in a hydrocarbon residue by a metal is not usual but in this case and in the case of **malonic acid** (p. 275), when a *methylene group*, ($\text{—CH}_2\text{—}$), is linked *between two carbonyl groups*, the hydrogens take on acid properties and are replaceable by metals, e.g., sodium.

Alkyl Derivatives.—When this sodium salt reacts with an alkyl halide the reaction is analogous to the **Wurtz** reaction, the sodium is exchanged for the alkyl radical, and an alkyl derivative of the ester is obtained.



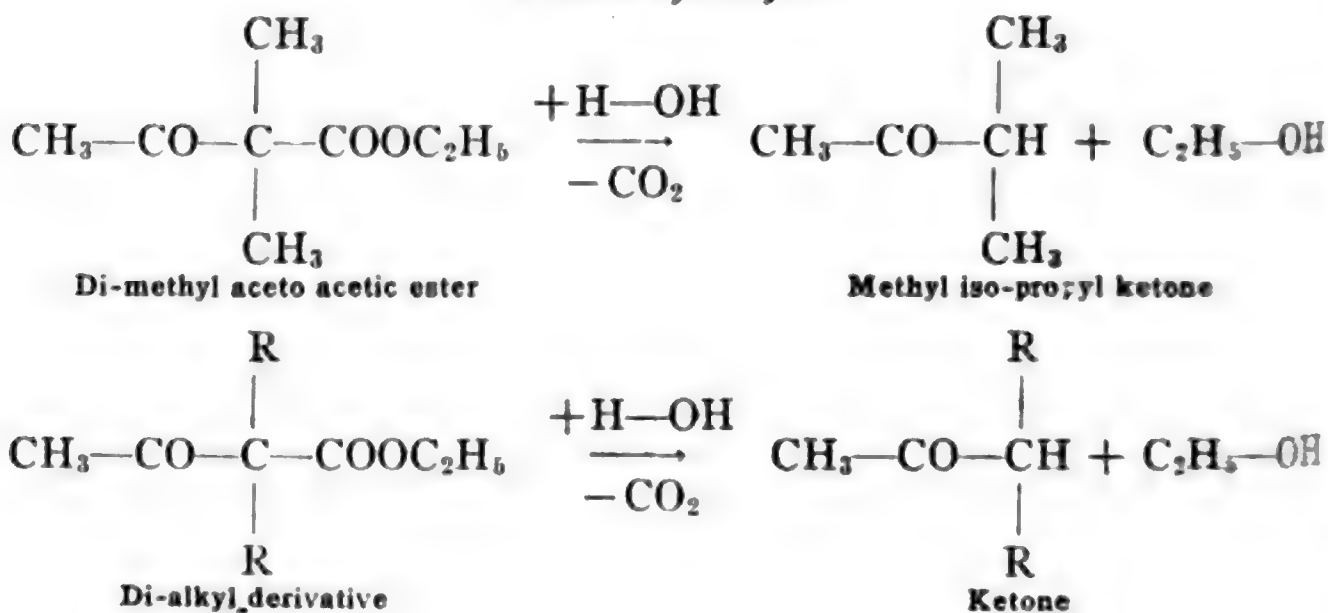
Such an alkyl derivative may then yield a new sodium salt and the sodium again be replaced by an alkyl radical and a *di-alkyl* derivative may be obtained.

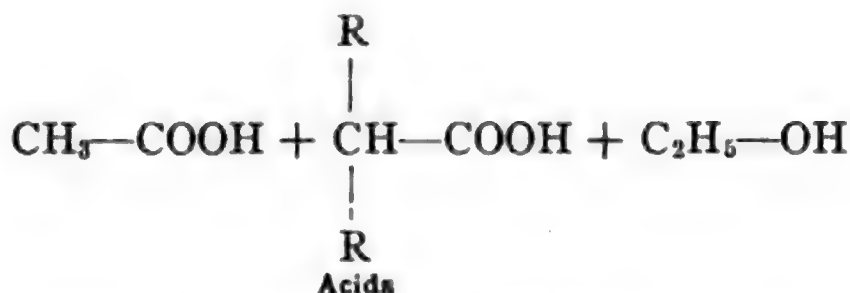
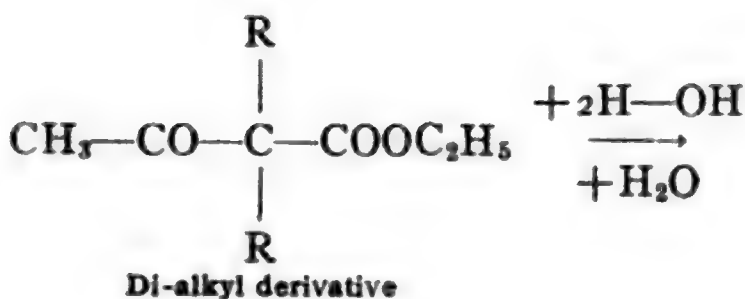
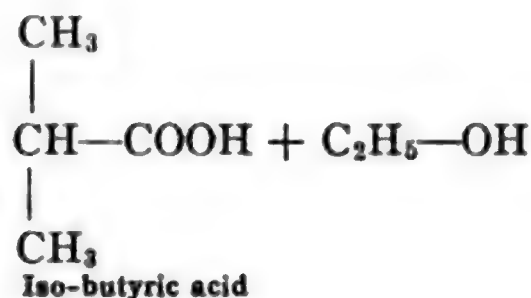
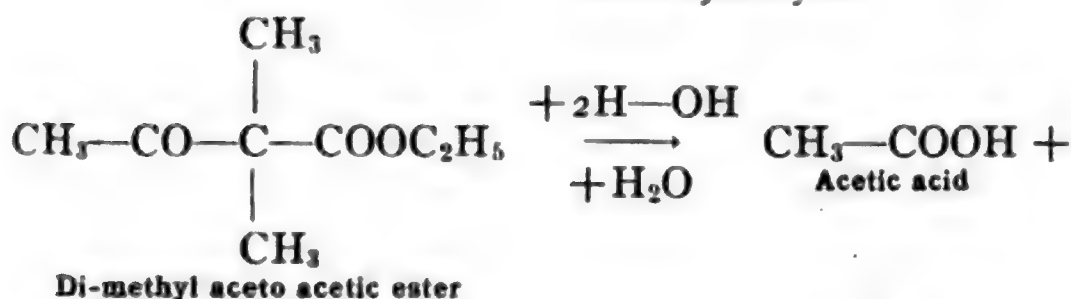


As the alkyl radical may be varied at will it becomes possible to introduce into the carbon group linked between the two carbonyl groups any one or any two radicals. Also the sodium salt reacts with *acyl halides* by which it becomes possible to introduce not only *alkyl* but also *acyl* radicals.

Aceto Acetic Ester Syntheses.—These alkyl and acyl derivatives of ethyl aceto acetate, both the mono- and the di- derivatives, react now on hydrolysis in the two ways given above, *i.e.*, by the *ketone hydrolysis* or the *acid hydrolysis* and we may thus obtain a large number of ketones and acids as desired.

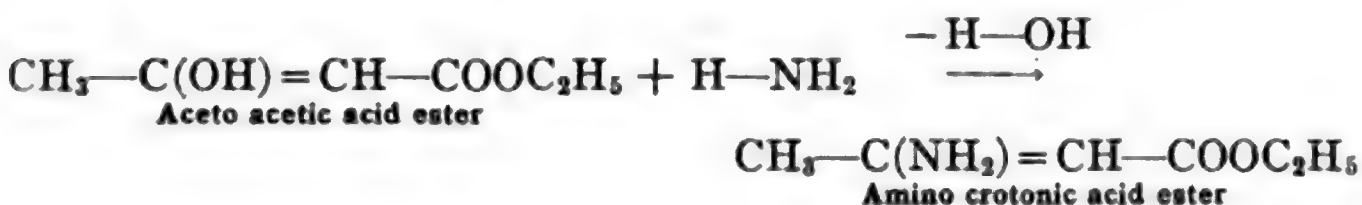
Ketone hydrolysis



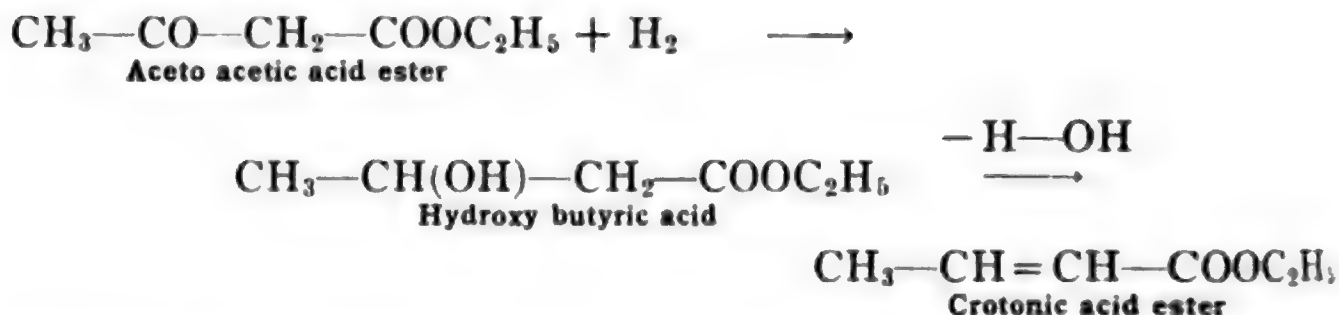
Acid hydrolysis

We thus see what a variety of ketones and acids are possible of synthesis by means of ethyl aceto acetate as not only the open chain compounds which we are studying but cyclic compounds and those containing nitrogen may result. Some of the important ones, *e.g.*, **anti-pyrine** will be mentioned later (Part II).

Action of Hydrogen and of Ammonia.—Another reaction of aceto acetic ester should be mentioned. When hydrogen (sodium amalgam), ammonia or alkyl primary amines react with aceto acetic ester, crotonic acid (p. 173) $\text{CH}_3\text{—CH=CH—COOH}$, or derivatives of it are obtained. The fact that crotonic acid contains a double bond seems to indicate the presence of a double bond in aceto acetic ester, and would be evidence for the *enol* form.



However, the reaction may be written also with the *keto* form as follows, in the case of the action of hydrogen.



Intermediate addition products are formed in both cases and in the last reaction the compound has been definitely proven to be β -hydroxy butyric acid.



We need simply mention briefly the simplest representative of the *gamma*-ketone acids. **Levulinic acid** derives its name from the fact that it is formed by the decomposition, with boiling dilute acids, of **fructose sugar** which is also known as **levulose**. It is in fact a characteristic product of similar decompositions of hexose sugars or higher carbohydrates which yield hexoses. The constitution as a ketone acid as given above has been established. It may also be termed **aceto propionic acid** and is isomeric with **methyl aceto acetic acid** (p. 257). It is a crystalline solid, soluble in water, melting at 33.5° and boiling at 250° . We shall refer to this compound later in connection with the synthesis of **rubber**.

IX. POLY-ALDEHYDES, POLY-KETONES AND POLY-CARBOXY ACIDS

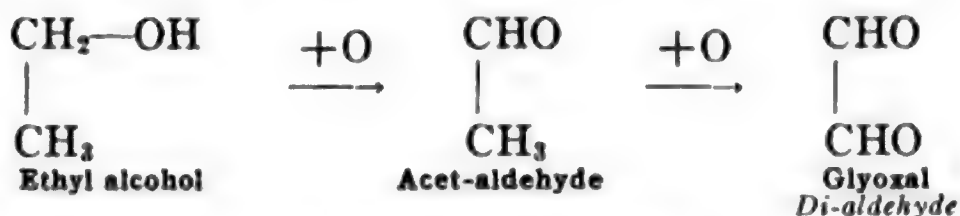
A. DI-ALDEHYDES AND DI-KETONES

We have considered poly-hydroxy alcohols and then mixed compounds such as halogen alcohols, halogen aldehydes, halogen acids, hydroxy acids, aldehyde acids and ketone acids. We have also mentioned but deferred the discussion of aldehyde alcohols and ketone alcohols and also of amino acids. Our next large group will be the *poly-carboxy acids* but before we consider them we should take up the two intermediate classes of di- or poly- compounds, viz., those containing two aldehyde or two ketone groups, *i.e.*, the *di-aldehydes* and *di-ketones*. There is also one more group of mixed compounds, viz., the *aldehyde ketone* compounds but these also in so far as they need to be considered will come in later in connection with the **carbohydrates**.

I. DI-ALDEHYDES

Glyoxal $\text{CHO}-\text{CHO}$

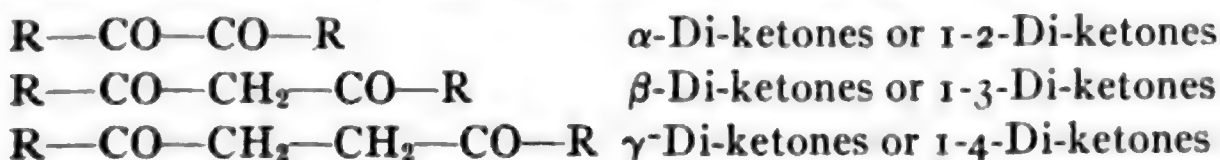
The simplest *di-aldehyde* possible is the one obtained by oxidizing ethyl alcohol or acetic aldehyde with nitric acid.



The di-aldehyde compound is known as **glyoxal**. It is obtained as a colorless, amorphous solid readily soluble in water. In all its reactions it possesses the properties of an aldehyde and its constitution and relationship are as represented above.

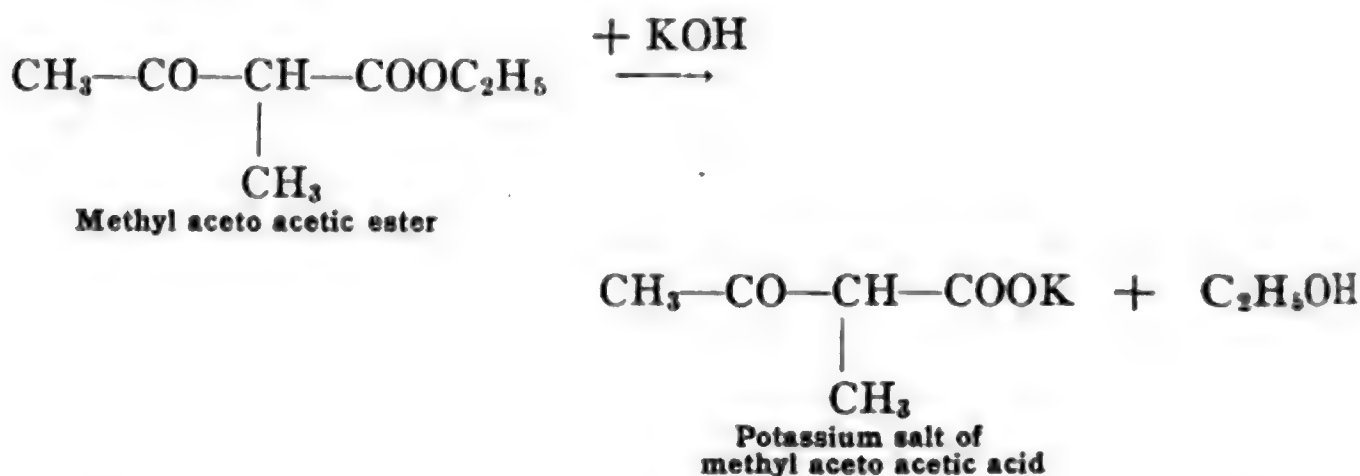
II. DI-KETONES

The *di-ketones* are similar to the ketone acids in being classified according to the relative position of the two carbonyl groups. We have, therefore, *alpha*-, *beta*-, *gamma*-, etc., di-ketones as follows.

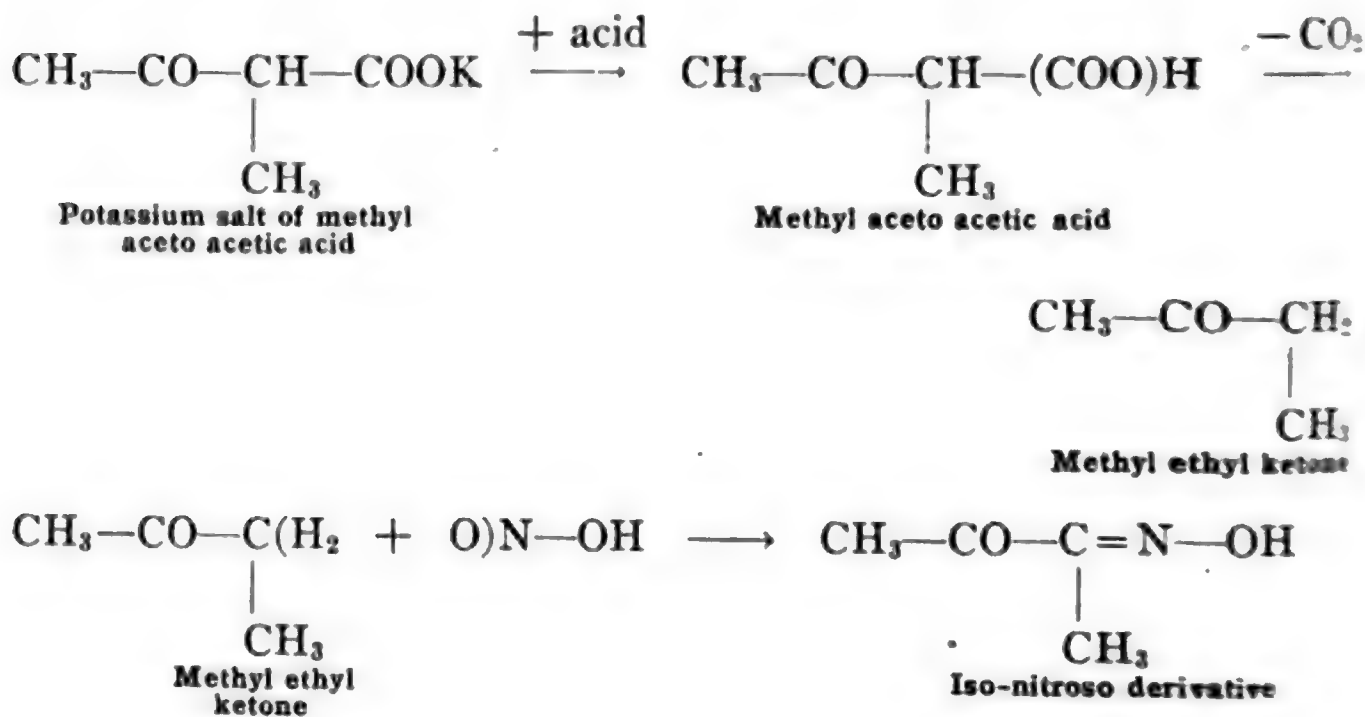


1-2-DI-KETONES Di-acetyl $\text{CH}_3\text{—CO—CO—CH}_3$.

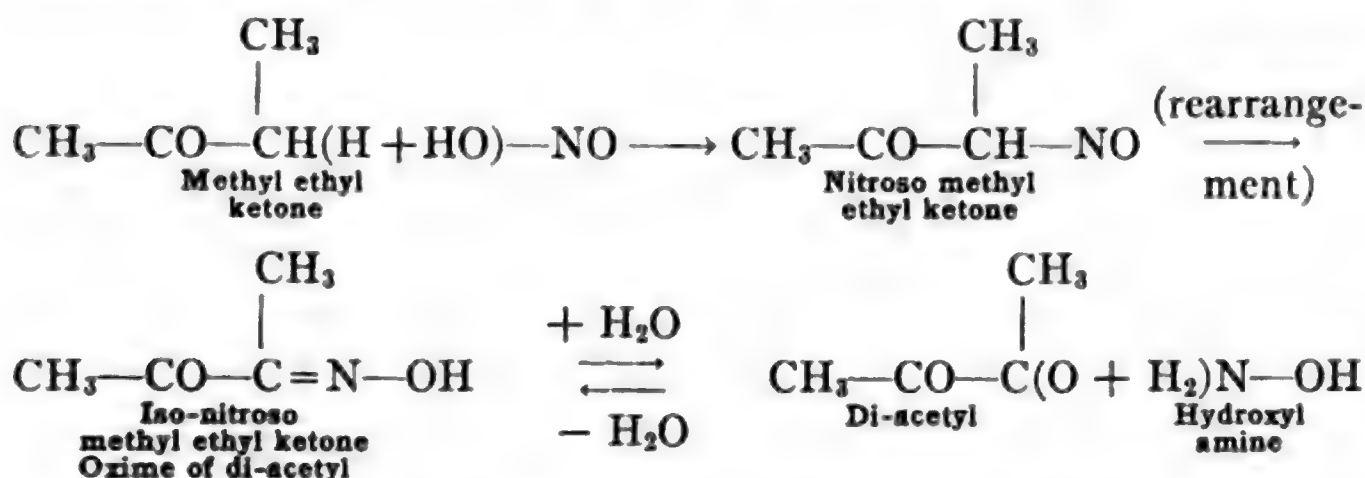
From Aceto Acetic Ester.—The simplest di-ketone, which is naturally an *alpha*-di-ketone, is $\text{CH}_3\text{—CO—CO—CH}_3$, **di-acetyl**. It is made from methyl aceto acetic ester by an interesting reaction involving the ketone hydrolysis. When aceto acetic ester is treated in the hot with dilute alkali the ketone hydrolysis takes place. If, however, the treatment is in the cold, hydrolysis results simply in the formation of the potassium salt.



When this salt is treated with nascent nitrous acid, HO—NO , the compound is first converted into the free acid which loses carbon dioxide forming a ketone. This ketone then reacts with the nitrous acid and the *oximino group*, ($=\text{N—OH}$), becomes linked to the carbon atom which was originally linked between the two carbonyl groups.



Iso-nitroso and Oxime Compounds.—This *iso-nitroso* derivative of the *mono-ketone* (methyl ethyl ketone) is also an *oxime* of the *di-ketone* (di-acetyl) as may be shown by the following relationships.

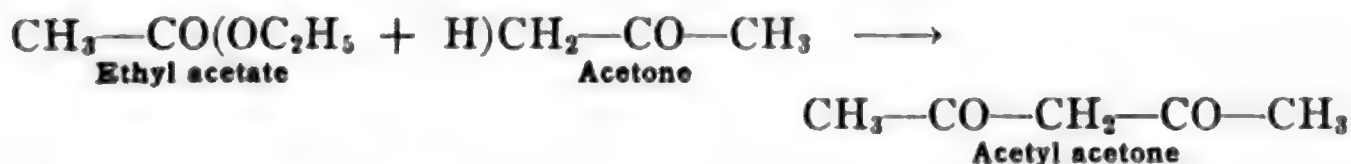


This rearrangement of *nitroso* derivatives into *iso-nitroso* derivatives or *oximes* is of especial importance in connection with the benzene compounds and a group of *nitroso* dyes. The oxime yields the di-ketone when hydrolyzed by boiling with dilute sulphuric acid, as above. **Di-acetyl**, being a di-ketone, reacts in all respects as a di-carbonyl compound especially in yielding both the *mono-oxime* as above and also a *di-oxime*.

1-3-DI-KETONES Acetyl Acetone $\text{CH}_3-\text{CO}-\text{CH}_2-\text{CO}-\text{CH}_3$

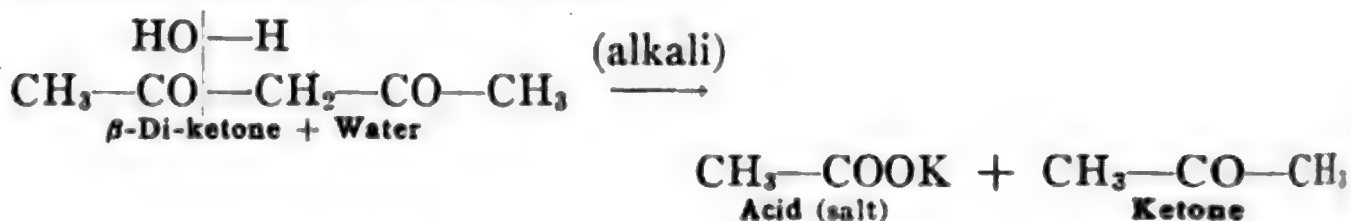
The *beta*-di-ketones are very similar to the *beta*-ketone acids both in their formation and reactions.

From Ethyl Acetate.—The simplest member of this group is $\text{CH}_3-\text{CO}-\text{CH}_2-\text{CO}-\text{CH}_3$ which is plainly **acetyl acetone**. It is best made by a reaction exactly analogous to the one used in preparing aceto acetic ester. In making the latter ethyl acetate is condensed with itself by means of sodium and ethyl alcohol (sodium ethylate) as described already (p. 254). If instead of condensing with another molecule of itself ethyl acetate condenses with **acetone** we obtain **acetyl acetone**, as follows:



By using any other methyl alkyl mono-ketone other *beta*-di-ketones may be obtained.

In these *beta*-di-ketones we have the same condition of the linkage of a *methylene group*, ($-\text{CH}_2-$), between *two carbonyl groups* as we had in the case of aceto acetic acid. The hydrogen atoms of this methylene group like the similar ones in aceto acetic ester are replaceable by metals, (sodium), and through these sodium compounds new alkyl or acyl radicals may be introduced. By boiling with alkalies the *beta*-di-ketones undergo a mixed acid and ketone hydrolysis and there is obtained both an acid and ketone.



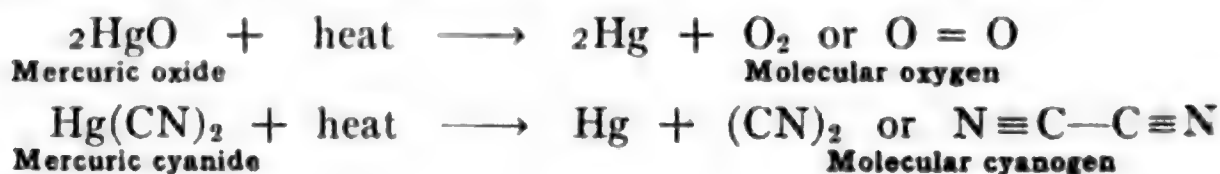
B. POLY-CARBOXY ACIDS

I. SATURATED DI-BASIC ACIDS

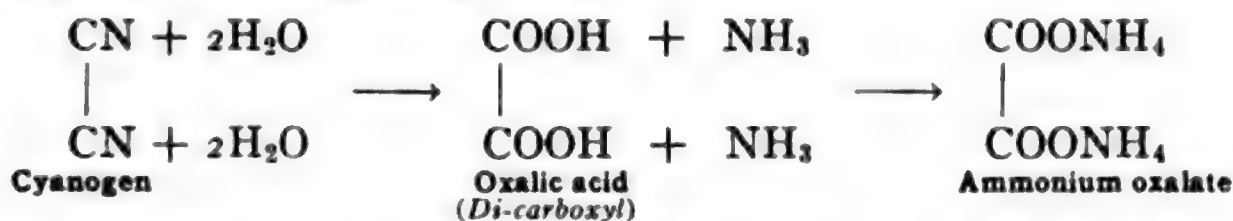
Corresponding to the poly-hydroxy or poly-acid alcohols are the *poly-carboxy* or *poly-basic acids*. The simplest of these poly-basic acids are those containing two carboxyl groups. Such compounds contain two acid hydrogens and are thus *di-basic*, exactly analogous to the di-basic inorganic acids, *e.g.*, sulphuric acid, $\text{HO} \text{---} \text{SO}_2 \text{---} \text{OH}$.



Synthesis from Cyanogen.—The simplest di-basic acid known is the common substance **oxalic acid**. Its composition corresponds to the formula $\text{H}_2\text{C}_2\text{O}_4$. The compound is definitely di-basic so that it must contain two acid hydrogens, *i.e.*, *two carboxyl groups*. As two carboxyl groups alone correspond to the formula given this would indicate that the constitution must be that of two carboxyl groups linked together, *i.e.*, $\text{HOOC} \text{---} \text{COOH}$. This constitution is also proven by its synthesis from **cyanogen**. Cyanogen has previously been mentioned as an example of a radical which exists as such. It is prepared from mercuric cyanide by heating, the reaction being exactly analogous to that of the formation of oxygen from mercuric oxide by heat. Cyanogen is thus analogous to molecular oxygen and is represented as $(\text{NC} \text{---} \text{CN})$. The two reactions may be represented as follows:

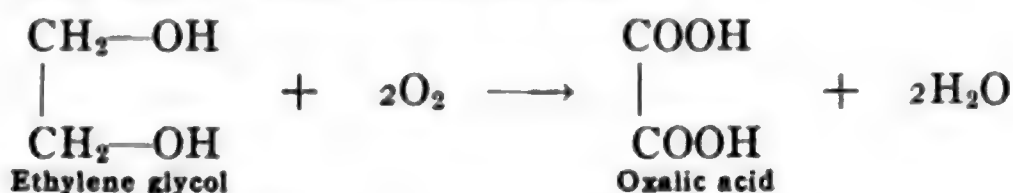


Hydrolysis of Cyanogen.—Organic compounds containing this cyanogen group, ($-\text{CN}$), yield acids on hydrolysis, hence they are called *acid nitriles* (p. 69). In this hydrolysis the cyanogen group, ($-\text{CN}$), is converted into the *carboxyl group*, ($-\text{COOH}$), and ammonia, NH_3 (p. 68). The hydrolysis of cyanogen gas would therefore yield *di-carboxyl*, as follows:

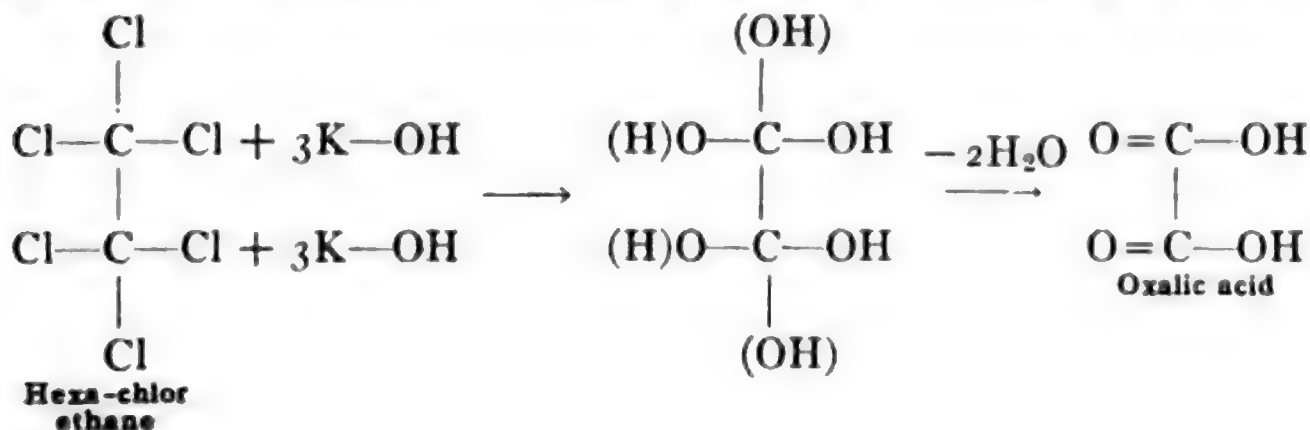


As oxalic acid is the product obtained by this hydrolysis it must have the constitution as represented, *i.e.*, it is *di-carboxyl*. In fact, when cyanogen is hydrolyzed ammonium oxalate is obtained which, of course, results from the combination of the oxalic acid and ammonia as first formed.

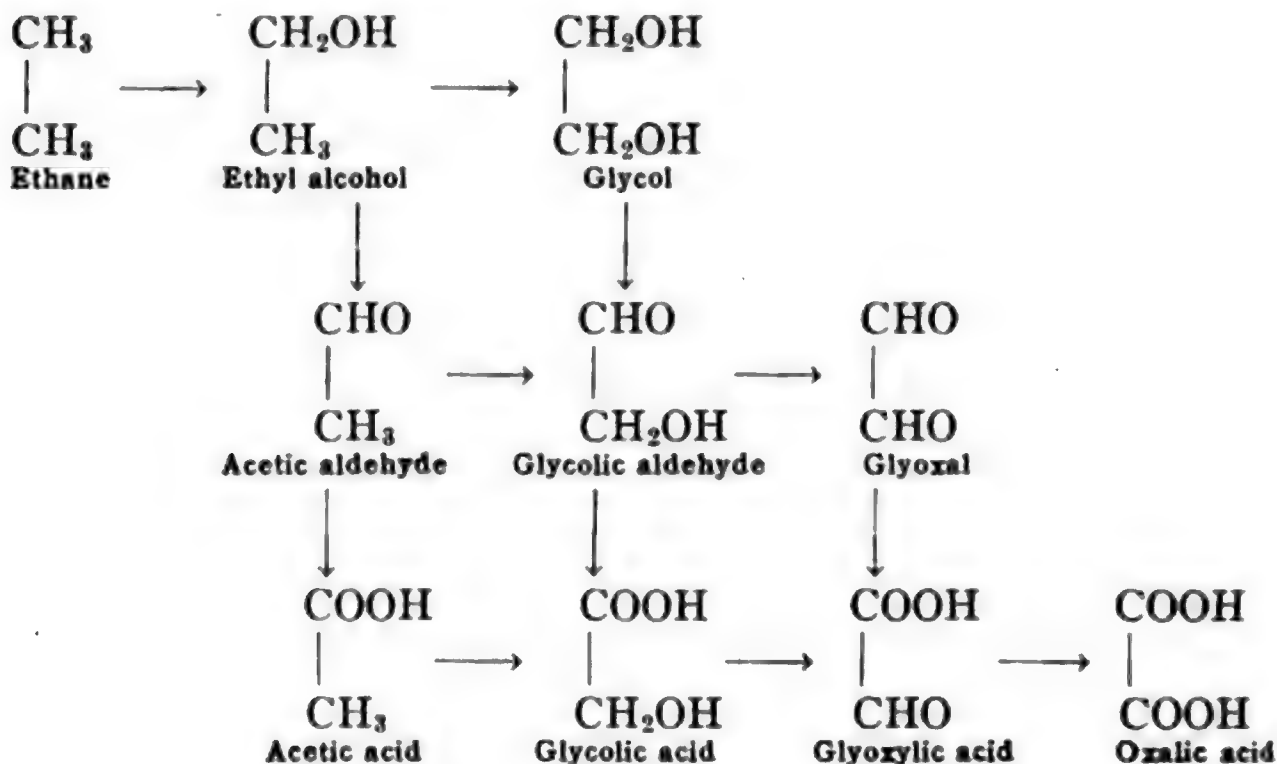
From Glycol.—A second synthesis which proves the constitution of oxalic acid is that from **ethylene glycol**, $\text{HO}-\text{CH}_2-\text{CH}_2-\text{OH}$. On the complete oxidation of glycol with nitric acid oxalic acid is obtained. This is plainly the oxidation of each of the primary alcohol groups to carboxyl, and may be represented as follows,



From Hexa-chlor Ethane.—It may also be prepared by oxidizing a derivative of ethane, viz., **hexa-chlor ethane**, C_2Cl_6 , with potassium hydroxide. This reaction may be considered as yielding the complete oxidation product of ethane by the replacement of the *six chlorine atoms* by *six hydroxyl groups*. This then loses water, as in the case of all compounds which contain more than one hydroxyl group linked to one carbon atom, and di-carboxyl, or oxalic acid results, as follows,



Oxidation Products of Ethane—Oxalic acid is thus the simplest di-carboxy acid possible. It may be considered as derived from ethane by the oxidation of both methyl groups to primary alcohol, aldehyde, and carboxyl groups successively. The entire series of oxidation relationships, including all of the intermediate compounds which we have already discussed, may be represented as follows:



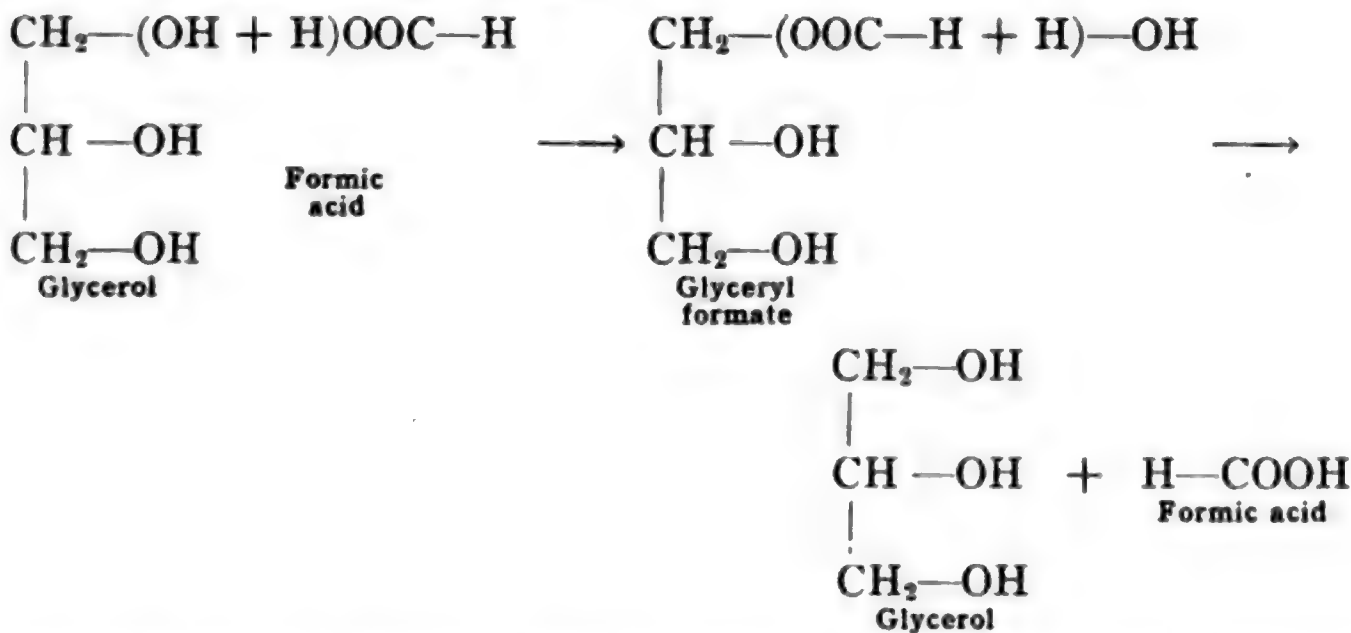
As each poly-hydroxy alcohol must have as many carbon groups as it has hydroxyls, so also, a poly-basic acid must have at least as many carbon groups as it has carboxyls and the simplest di-basic acid must be derived from the two carbon hydrocarbon.

Relation to Formic Acid.—The relation of oxalic acid to formic acid is shown by a series of important reactions. It will be recalled (p. 134), that formic acid may be made by rapidly heating oxalic acid, or by heating oxalic acid in glycerol. The reaction taking place is, in effect, simply the loss of carbon di-oxide, as follows,

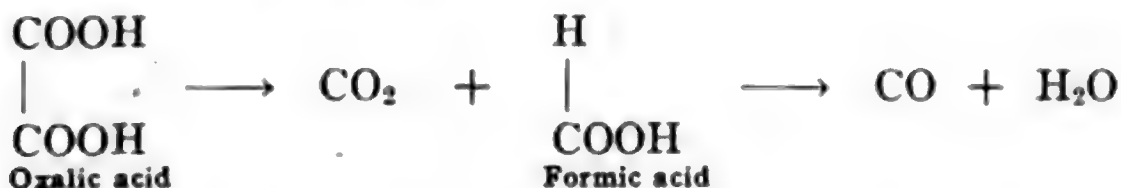


With glycerol the reaction takes place more easily and at a lower temperature, thus preventing the further breaking down of the formic acid. This is due to the intermediate formation of an ester of glycerol and formic acid. This ester is then hydrolyzed by the action of the water.

which is present as water of crystallization of the hydrous oxalic acid, and the formic acid is set free.

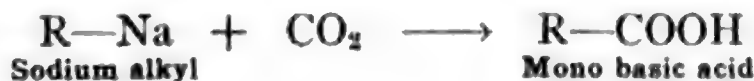


In this way the glycerol acts as a carrier of the formic acid and is used over and over just as is the case with the sulphuric acid in the preparation of ether. As formic acid breaks down by heating, and yields carbon monoxide and water, and oxalic acid, by similar treatment yields formic acid and carbon dioxide we may represent the complete breaking down of oxalic acid as follows,

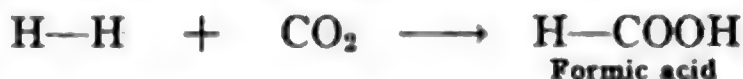


Therefore the final products of the decomposition of oxalic acid by heat are, **carbon di-oxide, carbon mon-oxide and water**. It will be recalled that, in elementary chemistry, the method of preparing carbon mon-oxide is by heating oxalic acid with sulphuric acid. The gaseous products are passed through a solution of potassium hydroxide to absorb the carbon di-oxide, and the resulting gas is pure carbon mon-oxide.

Reduction of Carbon Di-oxide.—This whole series of reactions shows us the relation that exists between carbon and its oxidation products, carbon monoxide CO, and carbon dioxide, CO₂. It has already been shown, that a general method for the preparation of mono-basic acids is by the action of carbon di-oxide upon the metallic alkyl compounds, as follows,



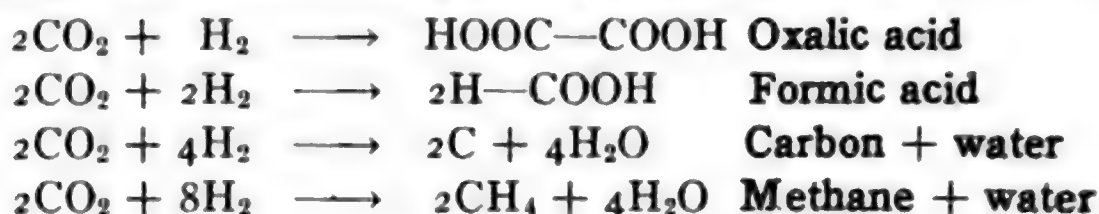
If hydrogen alone is used the product is formic acid,



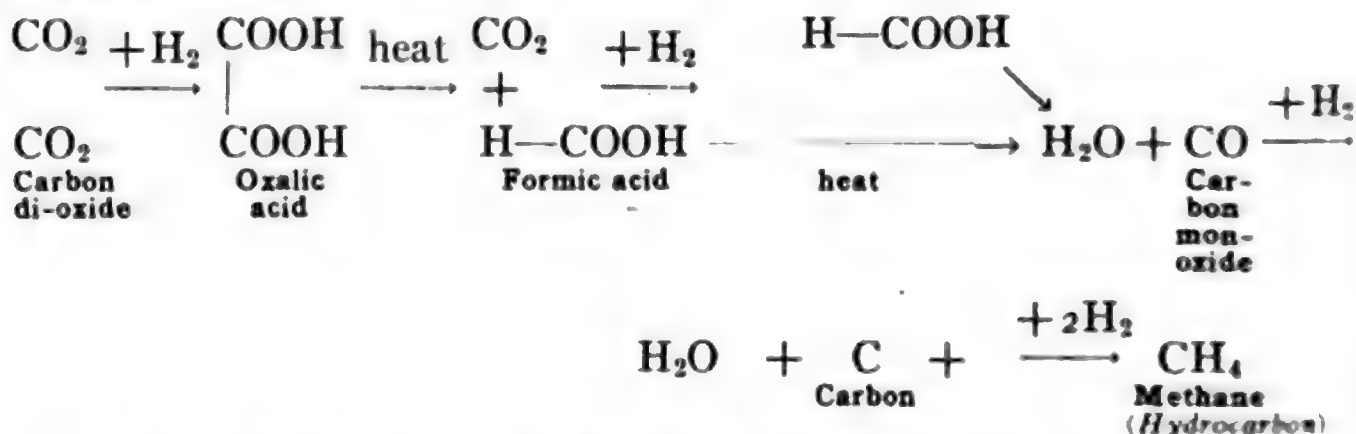
Now, sodium oxalate may be prepared by the action of carbon di-oxide upon sodium, at 360° ,



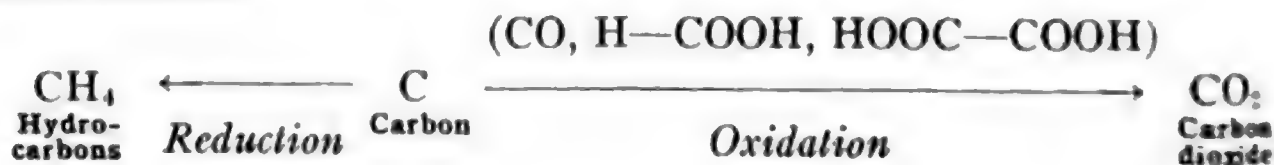
In this last reaction, it will be observed, twice as much carbon di-oxide is used as in the preceding reaction in the formation of formic acid from carbon di-oxide. Now, carbon mon-oxide and carbon are the reduction products of carbon di-oxide, and in the light of all of the reactions which we have just considered, we may represent the *theoretical stages in the reduction of carbon di-oxide*, as follows,



Or, as follows,

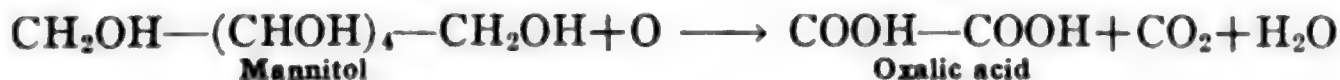


Thus, **carbon monoxide, oxalic acid and formic acid are intermediate products in the reduction of carbon di-oxide to elemental carbon.** If the reduction is continued beyond the stage of free carbon we shall obtain the *hydrocarbons* which stand at the other extreme to carbon di-oxide, in respect to the element carbon. The hydrocarbons are thus the reduction product and carbon dioxide the oxidation product of carbon. In other words the *final reduction products of carbon dioxide are hydrocarbons* and vice-versa the *final oxidation product of hydrocarbons is carbon dioxide*.



This relationship is illustrated by the fact, that both formic acid and oxalic acid are obtained by the oxidation of many organic substances, *e.g.*, wood, starch, sugar and alcohols, which are themselves, as has been explained in the case of alcohol, oxidation products of the hydrocarbons. Thus oxalic acid and formic acid stand close to carbon di-oxide, the final oxidation product of carbon, while the alcohols, sugar, starch and similar oxygen-containing organic substances, stand farther away from carbon di-oxide and closer to the hydro-carbons of which they are oxidation products. *This whole oxidation and reduction relationship of the element carbon is involved in the complicated bio-chemical reactions that occur in living plants and animals.* It will be somewhat clearer when we have studied the proteins and carbohydrates but the study of the function and properties of living cells and the associated catalytic action of enzymes is necessary for anything like a full understanding.

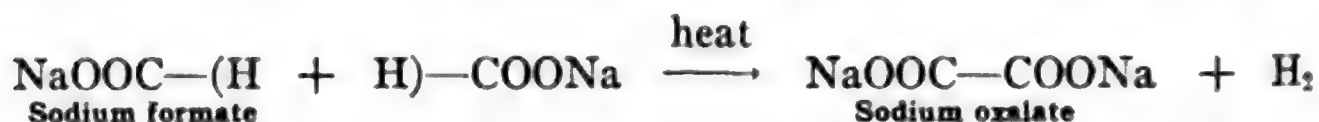
Commercial Preparation.—The commercial method for preparing oxalic acid, up to a few years ago, was by the oxidation of sawdust or sugar. In practice sawdust was oxidized by heating it with fused alkali by which process the alkali salt of oxalic acid was obtained. When sugar, or similar organic substances, like cellulose, are oxidized the reaction may be illustrated by the oxidation of the **hexa-hydroxy hexane**, or **mannitol**, as follows:



The two primary alcohol groups, *viz.*, the two end carbon groups, *become oxidized to carboxyl.* The intermediate *secondary alcohol groups become completely oxidized to carbon di-oxide and water* and are thus destroyed so that the two end groups yielding the two carboxyls become directly linked as oxalic acid. As the end carbon groups are the only ones capable of existence as primary alcohol groups and therefore able to yield carboxyl on oxidation, the reaction as above written is in accordance with both the facts and the possibilities.

Goldschmidt Process.—While this oxidation of organic substances was formerly the commercial method of preparing oxalic acid it has now been replaced by another process known as the **Goldschmidt Process.** This process rests upon the reaction, previously described, (p. 267), by which oxalic acid decomposes into formic acid and carbon di-oxide. When, however, formic acid, or better one of its salts, is

heated to 400° hydrogen is split off and practically the reverse of the above reaction occurs with the formation of oxalic acid as follows:



In the process as commercially carried out, the formic acid is first prepared from **carbon mon-oxide** and **sodium hydroxide** (p. 134).



This is accomplished by adding sodium hydroxide to heated coke and then passing over it a current of hot carbon mon-oxide. Also, instead of decomposing the formate at 400° it may be decomposed in the same way by heating to a lower temperature in sulphuric or phosphoric acid. Thus the simplest acids, in both the mono-basic and the di-basic series are each made from carbon mon-oxide and an alkali involving the reactions that have just been discussed and which show the relation which exists between the oxides of carbon and the two acids formic and oxalic.

Properties of Oxalic Acid.—Oxalic acid has been known from early times as the acid potassium and acid calcium salts in which form it is present in sorrel, or oxalis, and in other plants, especially rhubarb. In some cases, as in *Calladium* and in the *Jack in the Pulpit*, the calcium salt is present in crystalline form and gives to the plant a sharp prickly taste. Oxalic acid crystallizes from water in beautiful colorless mono-clinic prisms which are often of considerable length. The crystals contain two molecules of water of crystallization which are lost at 105° . The anhydrous acid melts at 189° and can be partially sublimed without decomposition. Its decomposition by heat, into formic acid has already been discussed. It is soluble in about 12 parts of water. It is a poison, and it has been claimed that its poisonous action is due to its breaking down and yielding carbon mon-oxide. With nitric acid oxalic acid is slowly oxidized to carbon di-oxide but with potassium permanganate, in acid solutions, it is very easily oxidized. This last reaction is the basis of the use of oxalic acid and its salts in volumetric analysis. The salts of oxalic acid are used as mordants in dyeing. The iron salts, because of their strong reducing properties, are used as photographic developers.

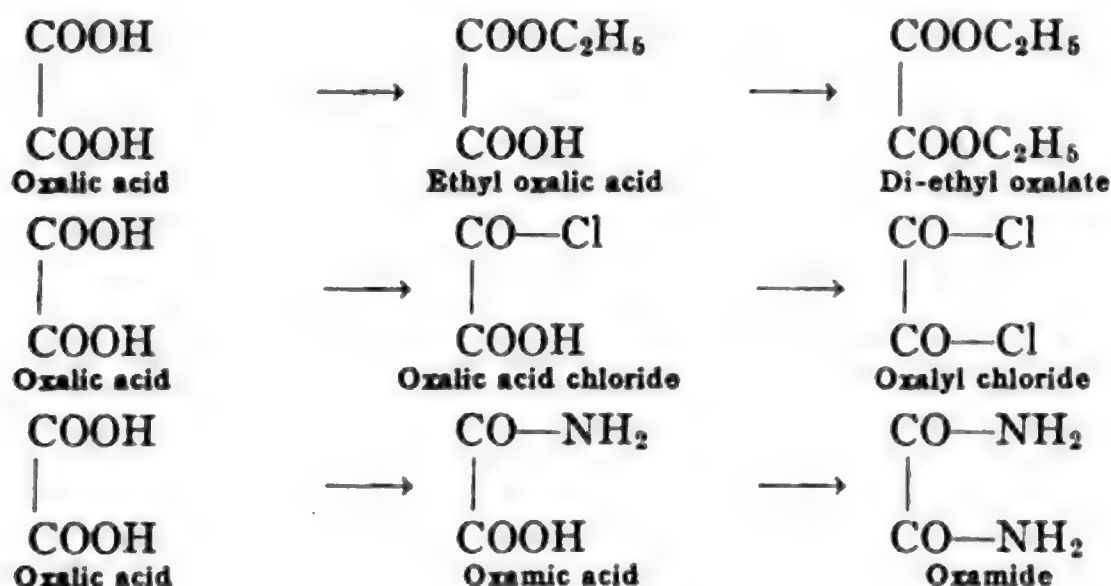
Derivatives of Oxalic Acid

Salts.—Oxalic acid forms two series of salts, due to its di-basic character, *i.e.*, the presence of two carboxyl groups. These are the *acid salts* and the *neutral salts*.

Acid Potassium Oxalate, $\text{KOO} \text{C} \text{---} \text{COOH}$.—This salt is the form in which oxalic acid occurs in sorrel. When obtained from this source, however, the acid salt combines with a molecule of free acid forming crystals with two molecules of water, *viz.*

Potassium Tetroxalate, $\text{KOO} \text{C} \text{---} \text{COOH} \cdot \text{HOOC} \text{---} \text{COOH} \cdot 2\text{H}_2\text{O}$.—This salt is also known commercially as *salt of sorrel*. The salts of oxalic acid with the alkali metals are more soluble in water than the free acid itself. Both the salts and the free acid dissolve iron rust and iron inks and are often used for the purpose of removing such substances from cloth.

Esters, Acid Chlorides, Acid Amides.—Just as oxalic acid, because of its di-basic character, forms two series of salts, it also forms two series of the other acid derivatives, *viz.*, *esters*, *acid chlorides* and *acid amides*.

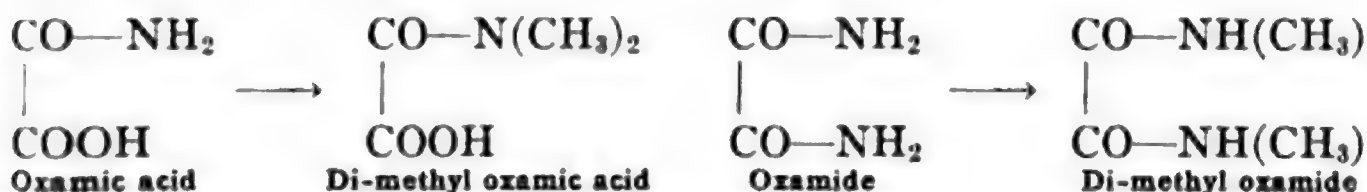


The *di-ethyl ester* of oxalic acid is easily prepared by heating anhydrous oxalic acid with absolute alcohol,



Di-ethyl oxalate is a liquid with a characteristic odor and which boils at 186° . **Ethyl oxalic acid, $\text{HOOC} \text{---} \text{COOC}_2\text{H}_5$,** is a liquid which boils at 117° , under 15 mm. pressure.

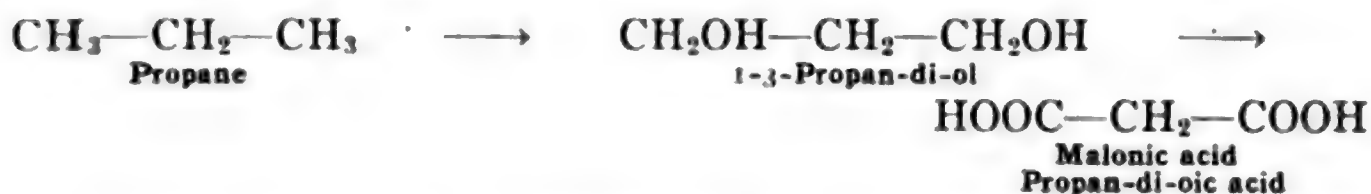
oxalic acid yield methyl substitution products in which the substitution is in the amino group.



Oxalic acid does *not* form an anhydride which is undoubtedly due to the space relations of the two hydroxyl groups.

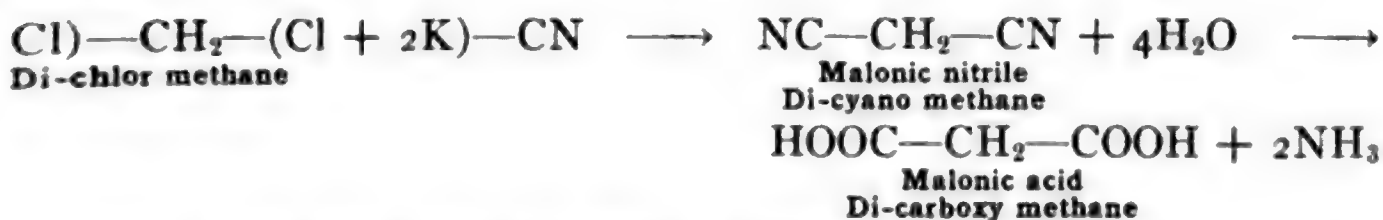
Malonic Acid $\text{HOOC—CH}_2\text{—COOH}$, **Propan-di-oic Acid**

Relation to Propane.—As oxalic acid, the simplest di-basic acid is derived from ethane the next higher member of the series should be derived from propane, C_3H_8 .

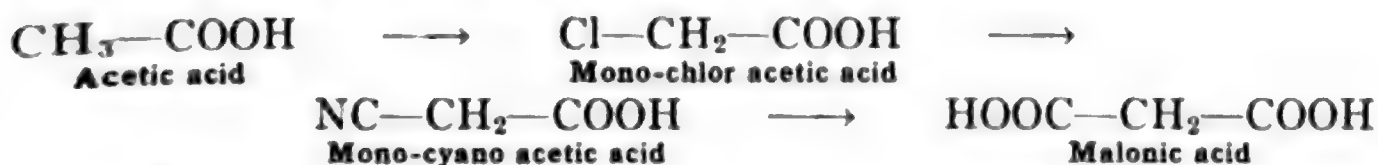


This acid is known as **malonic acid** and its systematic name, indicating its relation to propane, is **propan-di-oic acid**. As it may also be derived from methane by the substitution of two carboxyl groups, it is also known as **methane di-carboxylic acid**. It may similarly be regarded as a mono-carboxyl substituted acetic acid.

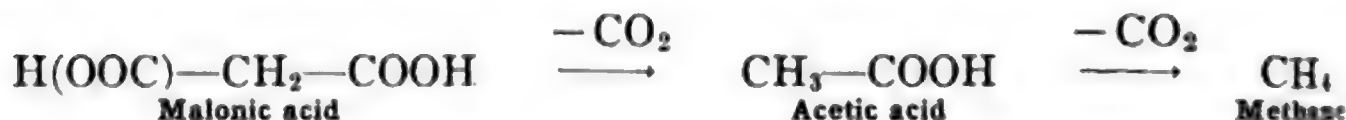
Relation to Methane and Acetic Acid.—The two syntheses of malonic acid which prove its constitution also show its relation to methane and to acetic acid as indicated above. **Di-cyano methane**, which is made from di-chlor methane by the action of potassium cyanide, yields malonic acid on hydrolysis and on that account is also known as **malonic nitrile**.



In a similar way **mono-chlor acetic acid** (p. 234) by means of potassium cyanide yields **mono-cyanogen acetic acid** and this on hydrolysis yields malonic acid, as follows:



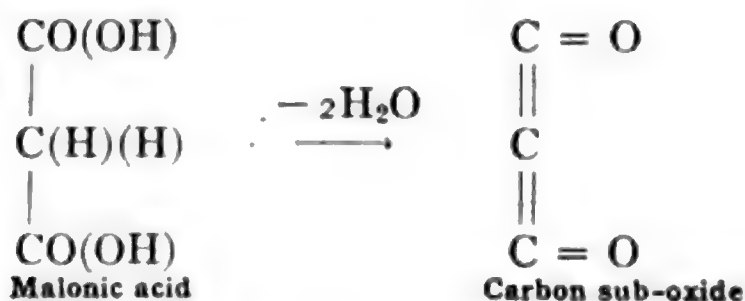
In a reverse way both acetic acid and methane may be obtained when malonic acid is heated just above its melting point, 140° – 150° . It loses one molecule of carbon dioxide and yields acetic acid which then by loss of a second molecule of carbon dioxide yields methane.



Thus the constitution of malonic acid is fully established as **di-carboxy methane** or **mono-carboxy acetic acid**, in accordance with the formula as given. It is really the first member of the homologous series of dicarboxy acids as it is the first one that contains a carbon-hydrogen group, ($\text{—CH}_2\text{—}$), just as acetic acid may be regarded as the first member of the homologous series of mono-carboxy acids. Formic acid and oxalic acid, neither of which contain a carbon-hydrogen group, may be considered as standing outside of the truly homologous series, though, of course, they are the simplest representatives of the mono- and di- basic acids.

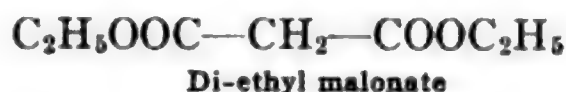
Homologues.—By substituting methyl or higher alkyl radicals into the group ($\text{—CH}_2\text{—}$) of malonic acid we obtain a series of homologous di-basic acids just as the homologous series of mono-basic acids are formed from acetic acid. Malonic acid is a solid crystallizing in triclinic plates which melt at 132° . It is soluble in water and in alcohol. It occurs in nature in sugar beets from which source it is obtained from the incrustation formed on the evaporating pans when beet sugar is made.

Reactions.—An important reaction of malonic acid is one that takes place when it is heated with strong dehydrating agents, *e.g.*, phosphorus pent-oxide, P_2O_5 . Two molecules of water are lost and carbon sub-oxide, C_3O_2 , is formed, as follows:

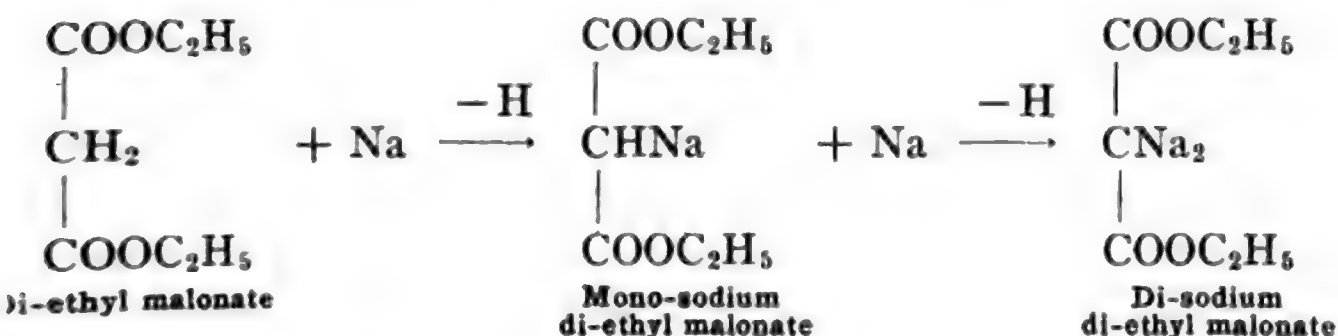


Malonic Acid Syntheses.—Malonic acid is one of the most important synthetic compounds in organic chemistry as it yields derivatives

that are very reactive. The derivatives which are most important and which lend themselves to synthetic reactions are the esters. Like all acids malonic acid yields esters readily. As a di-basic acid it yields both acid and neutral esters. It is the latter, however, which are the most important, *e.g.*,



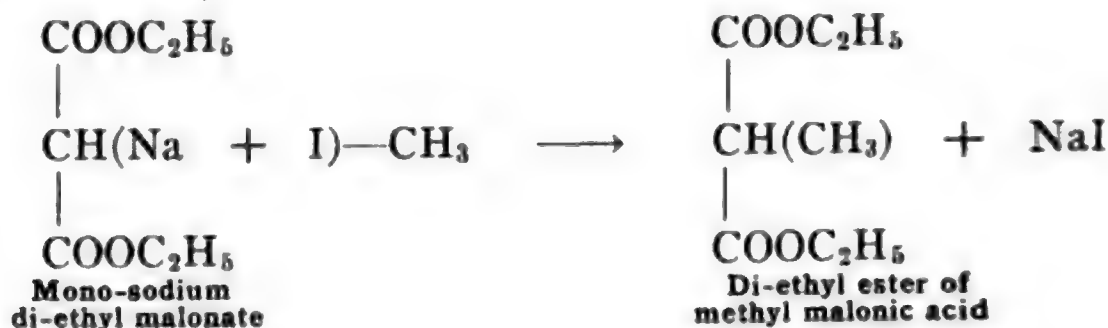
In these reactions the characteristic property of malonic acid and its esters rests in the *methylene group*, ($\text{—CH}_2\text{—}$). This same group we will recall is the reactive part of **aceto acetic ester** and we shall find that the linkage of the group is alike in the two compounds. When a carbon-hydrogen group is linked to *two carbonyl groups*, ($\text{C} = \text{O}$), or to *two carboxyl groups*, (—COOH), the latter containing the carbonyl group, the *hydrogen atoms of this carbon-hydrogen group possess distinctly acid properties*. This acid character of the hydrogen atoms of a methylene group so linked is shown especially in the reaction with metallic sodium, or with sodium alcoholate, as in the case of aceto acetic ester (p. 257). In this reaction hydrogen is liberated and the sodium enters the methylene group in its place, as follows:



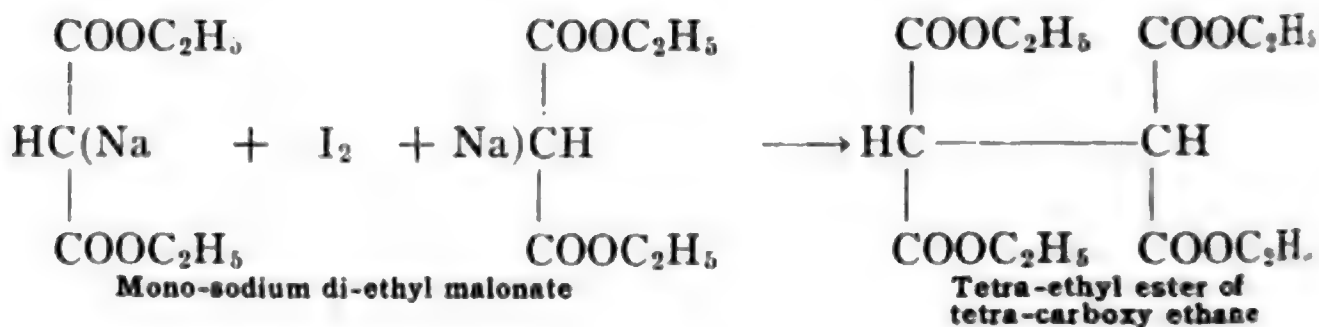
It will be recalled that sodium compounds of the alkyl radicals are of importance in the synthesis of hydrocarbons and acids.



In the case of malonic acid and other compounds when the methylene group is linked to two carboxyl groups the sodium compounds are more easily formed than are the sodium compounds of the alkyl radicals themselves. These sodium compounds of malonic acid ester, are especially reactive toward alkyl halides with the result that the *alkyl radical* is introduced into the malonic acid ester in place of the sodium, *i.e.*, in place of hydrogen of the methylene group. This is shown by the following reactions,

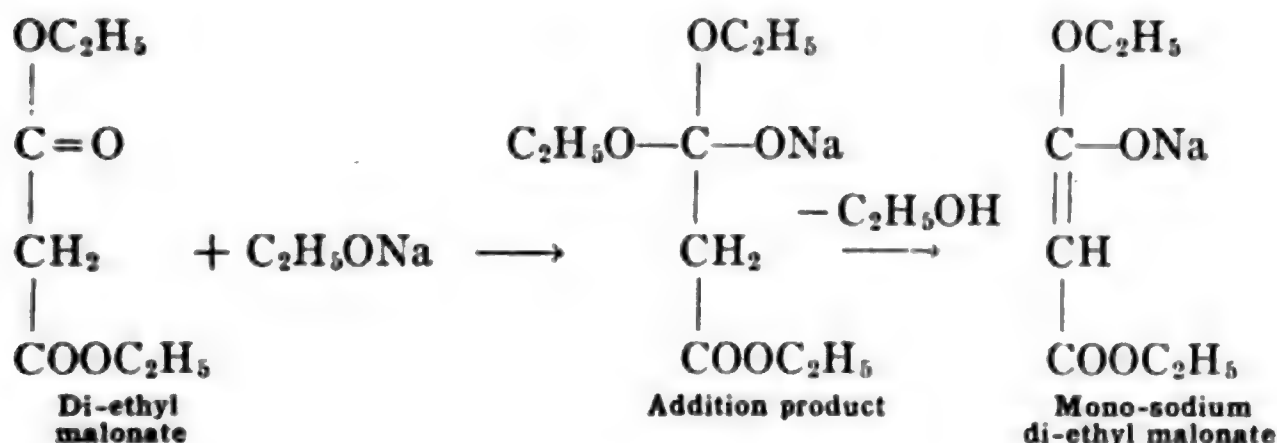


Thus, by these reactions, we may introduce into malonic acid a methyl radical, or by using any alkyl halide, $\text{I}-\text{R}$, we may *introduce any alkyl radical*. Now as the esters by hydrolysis yield the acids, and the di-basic acids by loss of carbon dioxide yield the corresponding mono-basic acids, which in turn, by loss of carbon dioxide, yield hydrocarbons, this general synthetic reaction gives us a means of preparing either homologous di-basic acids, corresponding mono-basic acids, or the corresponding hydrocarbons. Thus the *malonic acid syntheses*, or as they are also known, the *malonic ester syntheses*, are most important reactions for the general synthesis of any *mono-basic* or *di-basic* acid. Also, by reacting with halogens alone, two molecules of malonic acid are united into a condensation product and another type of compound, viz., a tetra-basic acid is formed, as follows:

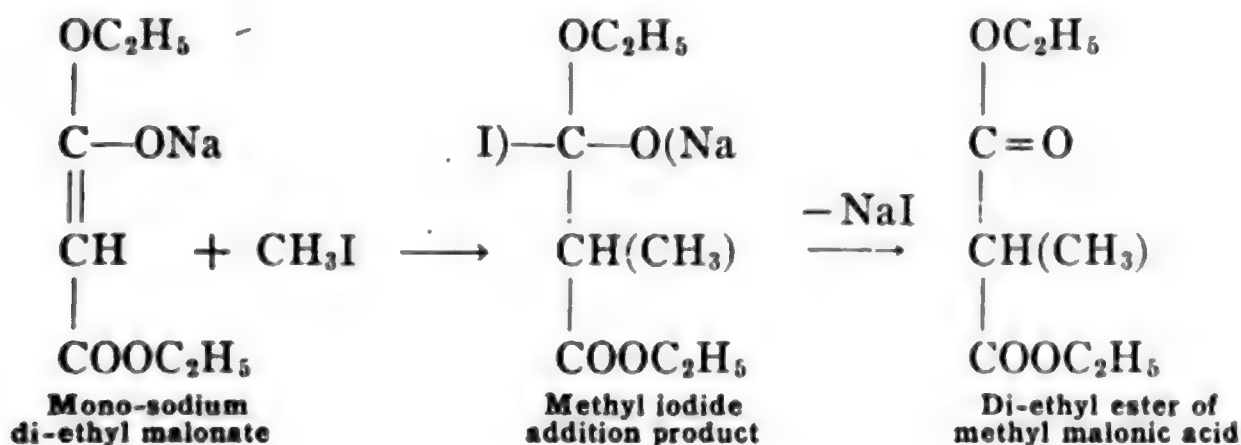


It is probable that the steps in these reactions take place in a different way than that indicated and exactly analogous to the similar

reactions of aceto acetic ester (p. 255). The reaction is carried out in alcohol and sodium alcoholate is first formed. This is then added on directly to the malonic acid ester, the addition product losing alcohol yielding a compound containing a double bond, as follows:



By this view the sodium malonic acid ester does *not have the same constitution* as the malonic acid ester itself. The sodium malonic acid ester containing a double bond now reacts with the alkyl halide and forms first an addition product similar to the one formed with the sodium alcoholate which then decomposes and yields the alkyl substitution product of the ester with the constitution first given.



Derivatives.—Of the salts of malonic acid only the alkali metal salts are soluble. The esters of malonic acid have been referred to as the most important derivatives. **Di-ethyl malonate** is a colorless insoluble liquid boiling at 198° . The **mono-sodium di-ethyl ester**, referred to in the above reactions, forms white glistening crystals. The **di-sodium di-ethyl malonate** forms gall-like masses and is easily decom-

posed. The di-acid chloride, **malonyl chloride**, and the di-amide, **malon-amide**, are both known.

Malonyl chloride, $\text{Cl}-\text{OC}-\text{CH}_2-\text{CO}-\text{Cl}$.

Malon-amide, $\text{H}_2\text{N}-\text{OC}-\text{CH}_2-\text{CO}-\text{NH}_2$.

Malonic acid does *not* yield an anhydride.

Homologues of Malonic Acid

Several of the homologues of malonic acid are known and they may all be prepared by the malonic ester synthesis as described above. A few of these will be mentioned simply by giving their formulas.

$\text{CH}(\text{CH}_3) = (\text{COOH})_2$ **Methylmalonic acid. Iso-succinic acid.**

$\text{CH}(\text{C}_2\text{H}_5) = (\text{COOH})_2$ **Ethyl malonic acid.**

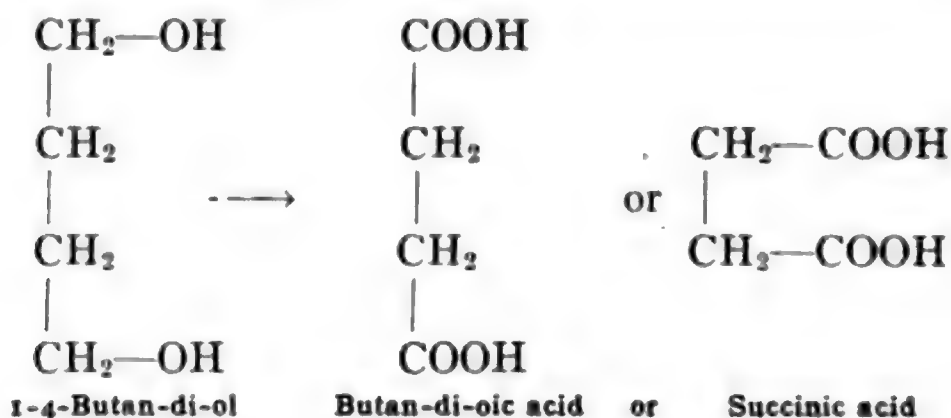
$\text{CH}(\text{C}_3\text{H}_7) = (\text{COOH})_2$ **Propyl malonic acid.**

$\text{CH}(\text{CH}(\text{CH}_3)_2) = (\text{COOH})_2$ **Iso-propyl malonic acid.**

$\text{H}_3\text{C}-\text{C}(\text{C}_2\text{H}_5) = (\text{COOH})_2$ **Methyl-ethyl malonic acid.**

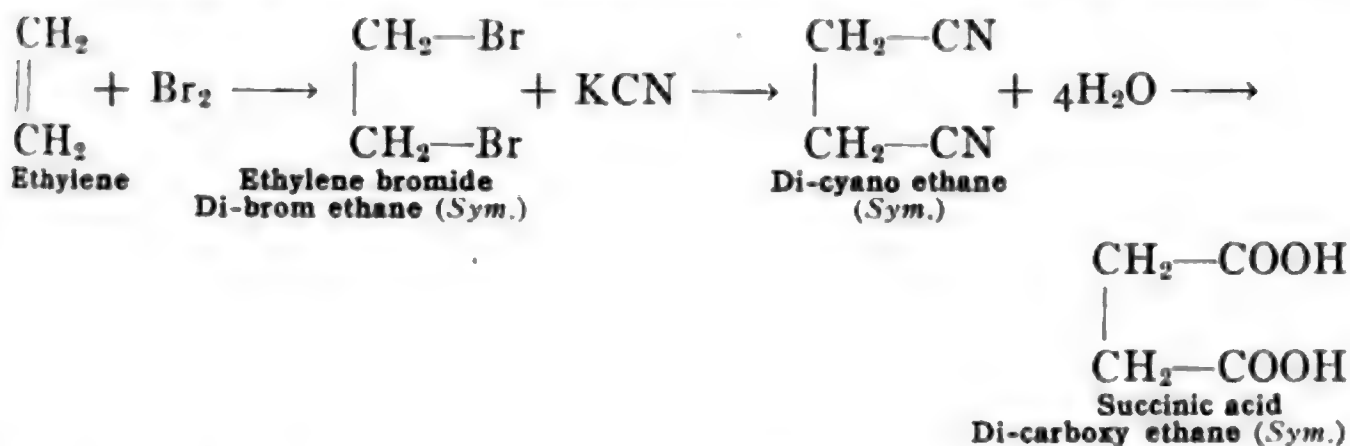
Succinic Acid $\text{HOOC}-\text{CH}_2-\text{CH}_2-\text{COOH}$. **Butan-di-oic Acid**

As oxalic acid is derived from ethan-di-ol, ethylene glycol, and malonic acid is derived from 1-3-propan-di-ol, so the next member in such a series will be derived from 1-4-*butan-di-ol*, as follows:



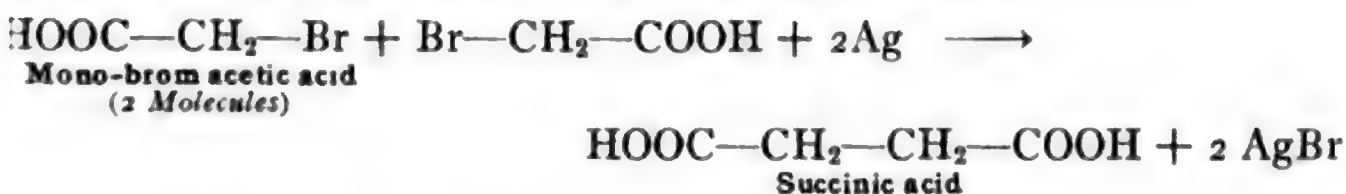
Synthesis from Ethylene Bromide.—Such an acid is known as a commonly occurring substance in nature and is called **succinic acid**. It has the composition $\text{C}_4\text{H}_6\text{O}_4$ and is plainly isomeric with **methyl malonic acid**. Its constitution as given above is, however, proven by the following syntheses: **Ethylene bromide**, or **symmetrical di-brom ethane**, which is made by the addition of bromine to ethylene gas, yields by treatment with potassium cyanide a **symmetrical di-**

cyano ethane, or ethylene cyanide. This compound is also called **succinic nitrile** because it yields succinic acid on hydrolysis, as follows:



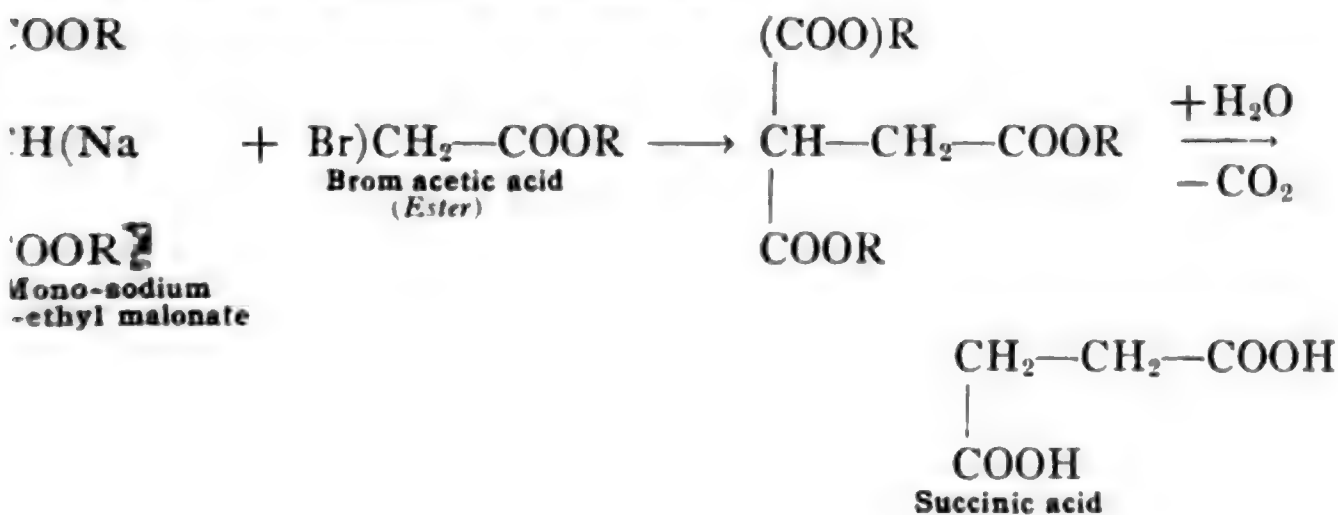
Therefore, succinic acid is **symmetrical di-carboxy ethane**.

From Brom Acetic Acid.—Also, **mono-brom acetic acid**, $\text{Br}-\text{CH}_2-\text{COOH}$, by the condensation of two molecules, with the elimination of the halogen by means of silver, yields succinic acid, as follows:



Di-acetic Acid.—By this synthesis, succinic acid must be two molecules of acetic acid joined together by the loss of one hydrogen from each molecule. It is therefore a symmetrical compound consisting of two like residues of acetic acid, $(-\text{CH}_2-\text{COOH})$, *i.e.*, **di-acetic acid**.

From Malonic Ester.—The same constitution is also proven by an interesting synthesis from malonic ester. **Mono-sodium di-ethyl malonate** reacts with monobrom, or mono-iodo acetic acid, and yields the ester of a tri-carboxy acid which after hydrolysis to the acid loses carbon di-oxide and yields succinic acid.



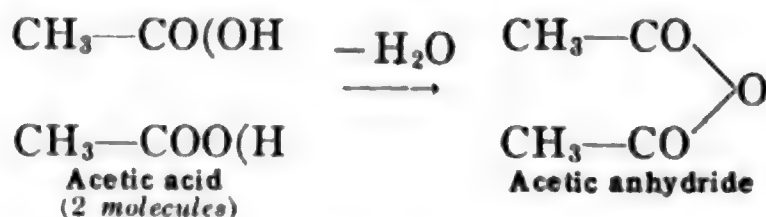
Thus, according to these two syntheses succinic acid must be *symmetrical di-acetic acid*. As succinic acid is isomeric with methyl malonic acid the latter is also called **iso-succinic acid**.

Properties.—Succinic acid has been known for a long time. It is quite widely distributed in nature. It is found in unripe fruits, especially in grapes, also in lignite, in peat and in many plants. Its most important occurrence is in *amber* from which it may be obtained by distillation. It is also a constituent of wines where it is the product of the alcoholic fermentation of the sugars of grape juice. Another source, which will be considered later, is from **malic** and **tartaric acids** by bacterial or mould fermentation. Succinic acid crystallizes in plates or columns which melt at 182° . It sublimes when it is heated below its melting point. When heated rapidly to 235° it loses water and forms an *anhydride*. It is soluble in 14 parts of water.

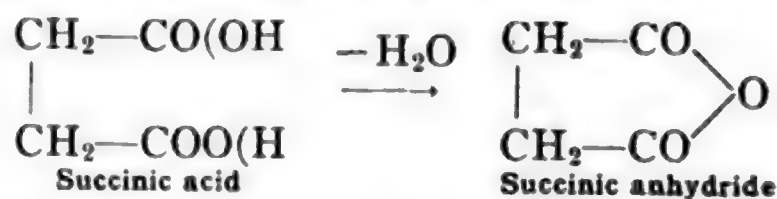
Derivatives of Succinic Acid

Salts.—The salts of succinic acid are not of especial importance. The basic ferric succinate is used in the analytical separation of iron, zinc, manganese, cobalt and nickel. As stated above when succinic acid is heated rapidly to 235° it loses water and forms an *anhydride*.

Anhydride.—In considering the mono-basic acids it was stated that acetic acid formed an anhydride by the loss of *one* molecule of water from *two* molecules of the acid, as follows:



Succinic acid, however, forms an anhydride by the loss of *one* molecule of water from *one* molecule of the acid, as follows:



Succinic anhydride is thus an *inner anhydride* and the *open chain* compound is changed into a *ring* or *cyclic* compound. This is of especial importance in connection with the relation between open chain and cyclic compounds as will be pointed out later when we consider the

latter class. The formation of this inner anhydride compound and of a similar inner anhydride, or de-ammoniated compound, from the amide of succinic acid, is of especial importance in connection with the tetra-hedral theory of the carbon atom. None of the other di-basic acids thus far mentioned, viz., oxalic acid or malonic acid, or the homologues of the latter, form these inner anhydrides. When a chain of four tetra-hedral carbon groups, of which the end carbons are carboxyl groups, is constructed with models, or by drawings, it will be seen that the space relations of the two carboxyl groups are such that the two hydroxyls come very close together. This is shown by the accompanying drawing.

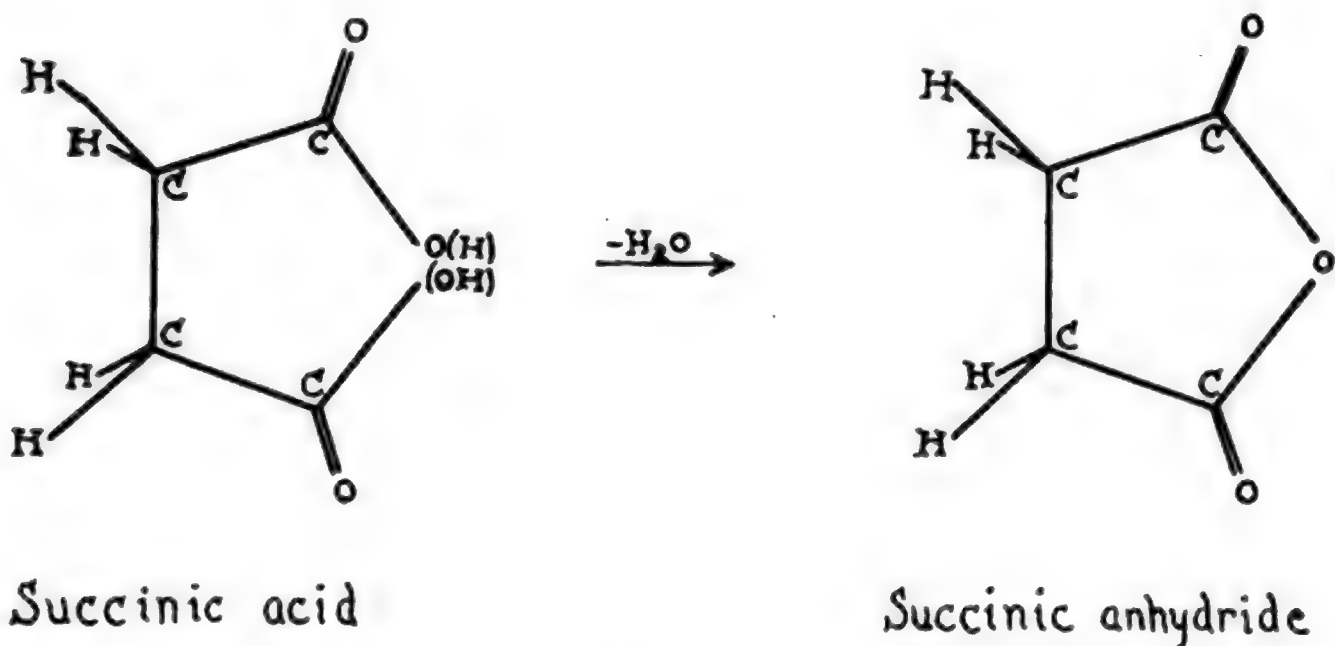
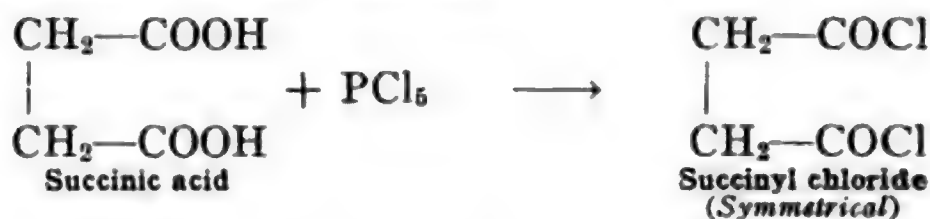


FIG. 5.

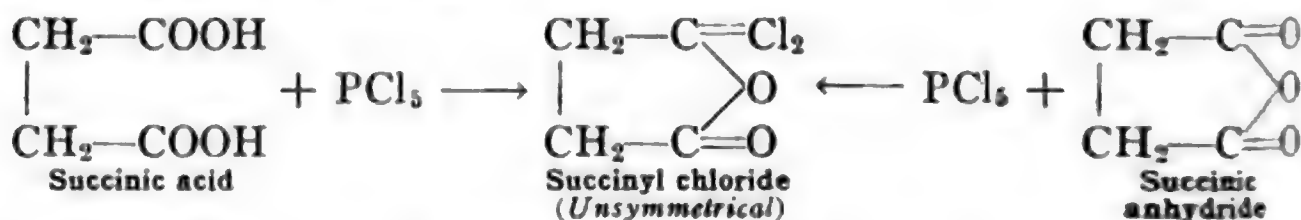
With oxalic acid, which has only two carbon groups, both of which are carboxyl, or with malonic acid which has three carbon groups, it is found that the hydroxyls of the two carboxyl groups are some distance apart and that the tendency to lose water and form anhydrides does not exist as shown by the fact that anhydrides are not known. If a fifth carbon group is introduced into succinic acid, as is the case in **glutaric acid**, which we shall presently consider, we find that the two carboxyl groups at the end of the chain of five carbons practically touch each other and the formation of an anhydride in the case of this acid takes place even more readily than with succinic acid. This interesting space relation will be considered again when we come to the study of the cyclic compounds. Succinic anhydride may also be formed

from succinic acid by the action of dehydrating agents, *e.g.*, phosphorus oxy-chloride, POCl_3 , when heated with it to $100^\circ\text{--}120^\circ$. **Succinic anhydride** forms crystals which melt at 116.5° and boil at 261° . The anhydride dissolves in water reforming the acid.

Acid Chlorides.—As succinic acid is a di-basic acid it forms a *di-chloride* when the acid, or the anhydride, is treated with phosphorus penta-chloride, PCl_5 . *Two* compounds result, however; one, which is formed in much smaller amount, has been shown to be analogous to the chloride of malonic acid, malonyl chloride. It is known as the **symmetrical succinyl chloride**.

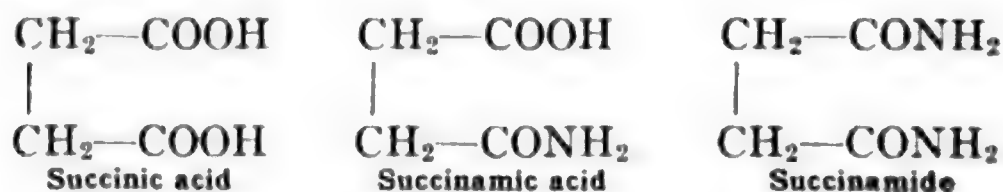


This **symmetrical succinyl chloride** is a crystalline compound which melts at 190° . By far the greater part of the product of the action of phosphorus penta-chloride upon succinic acid is not the compound above mentioned but another to which an *unsymmetrical* formula has been given, as follows:

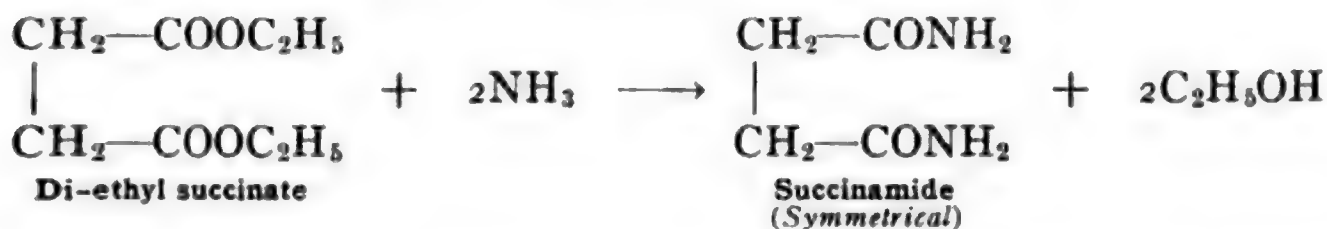


If the reaction is written with the anhydride instead of the acid itself it will be seen that the action consists in *two chlorine atoms* of the phosphorus penta-chloride *replacing one of the carbonyl oxygens*, of the acid. This replacement of one oxygen by two chlorines is, we know, the true reaction of phosphorus penta-chloride (p. 81). We shall find, also, that this reaction and the unsymmetrical compound formed are similar to reactions and compounds which we shall consider in the study of the benzene di-basic acid, **phthalic acid**.

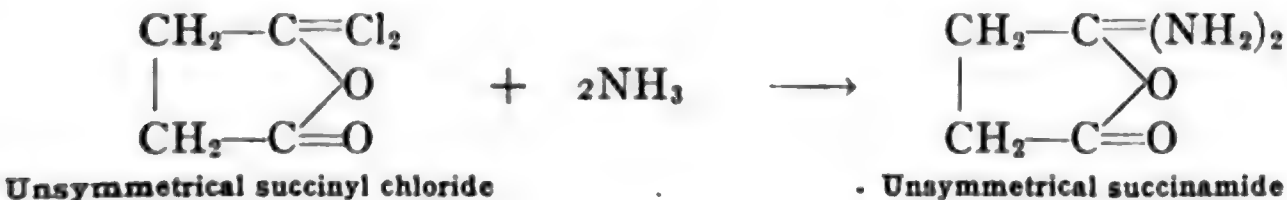
Acid Amides.—Succinic acid, like oxalic acid, forms both a *mono-* and a *di-amide*.



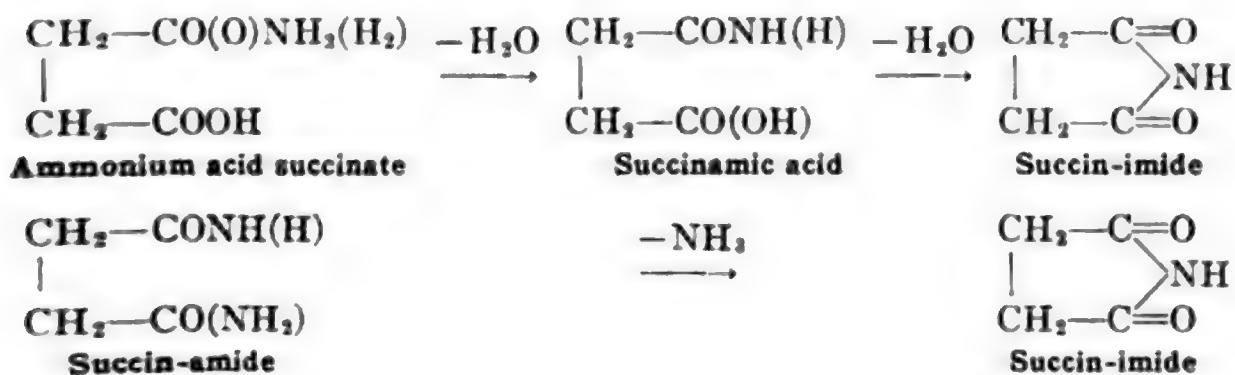
The mono-amide, **succinamic acid**, crystallizes in needles which melt at 156° . Like the di-chloride the di-amide of succinic acid also exists in *two isomeric forms*, viz., the *symmetrical* and the *unsymmetrical*. When di-ethyl succinate is treated with ammonia, **succinamide** is obtained. This compound is crystalline and melts at 242° .



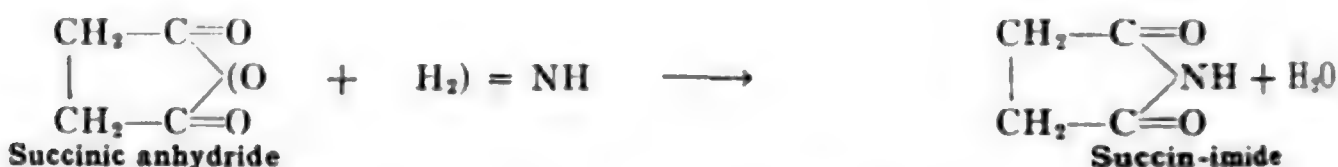
If, however, the di-amide is prepared by treating the *di-chloride* with ammonia another compound is obtained. As just stated, when the di-chloride is prepared the product is a mixture of two compounds, viz., the symmetrical and the unsymmetrical succinyl chlorides. This mixture of di-chlorides yields, by treatment with ammonia, a similar mixture of the **symmetrical succinamide**, just described, and another compound which is non-crystalline and which melts at 90° . To this latter compound the *unsymmetrical* structure has been given



Imide.—When ammonium acid succinate is heated water is lost in two steps. First, succinamic acid is obtained and then an *anhydride* compound. The same compound is also obtained when the *symmetrical di-amide* is heated and a *molecule of ammonia* is lost. The compound has been shown to have an *inner anhydride structure* exactly analogous to succinic anhydride and is known as **succin-imide**. The reactions may be represented as follow:



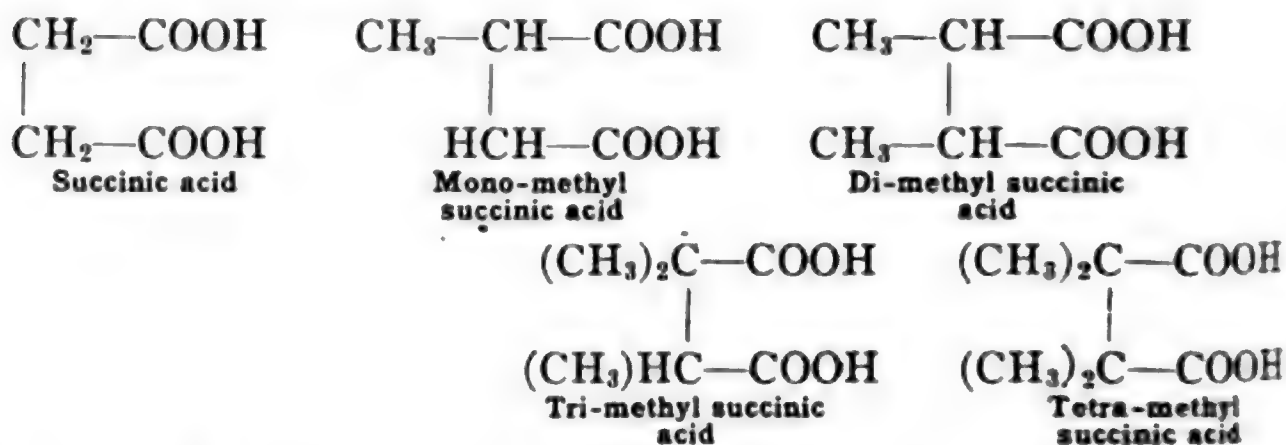
The compound is also formed by the action of ammonia upon succinic anhydride,



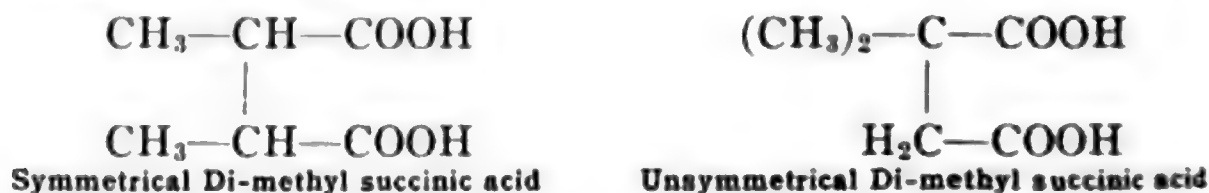
Succin-imide is soluble in water and forms crystals with one molecule of water of crystallization. The water-free succinimide melts at 126° and boils at 288° .

Homologues of Succinic Acid

The homologues of succinic acid are analogous to those of malonic acid and are formed by the introduction of alkyl radicals into the carbon groups that are not carboxyl in character. As succinic acid contains two such carbon groups, each of which has two replaceable hydrogens, we may have the introduction of one, two, three or four alkyl radicals. Taking, as an illustration, the methyl substitution products of succinic acid we may have the following compounds:



Mono-methyl succinic acid is known also as **pyro-tartaric acid** as it is formed from **tartaric acid** by heating. While the *mono*-, *tri*-, and *tetra*-methyl succinic acids can plainly be of only *one* type, the **di-methyl succinic acid** may exist in the *two* forms, viz., the symmetrical and unsymmetrical, as follows,

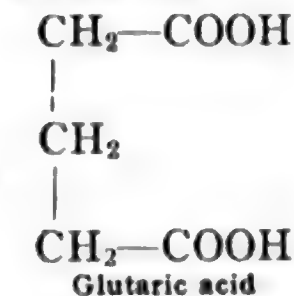
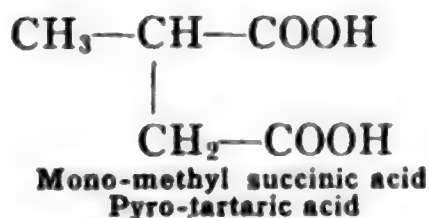
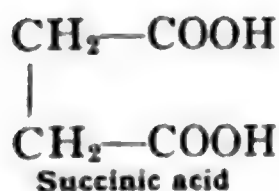
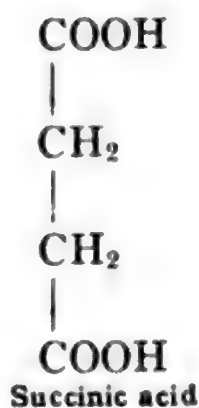
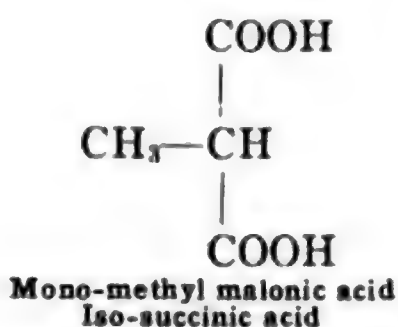
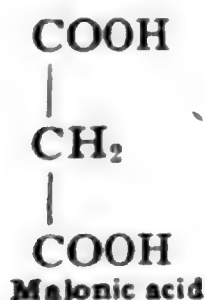


Both of these di-methyl succinic acids are known. The symmetrical compound boils at 197° and the unsymmetrical at 139° . On further

examination of the symmetrical di-methyl succinic acid formula it will be noticed that it possesses *two asymmetric carbon atoms*. Thus we have two structurally isomeric di-methyl succinic acids, the symmetrical and the unsymmetrical, and the former exists also in *stereo-isomeric forms*. The discussion of such stereo-isomeric forms is better considered when we study the related compound **tartaric acid** and further consideration will be postponed until that time.

Glutaric Acid $\text{HOOC}-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{COOH}$. **Pentan-di-oic Acid**

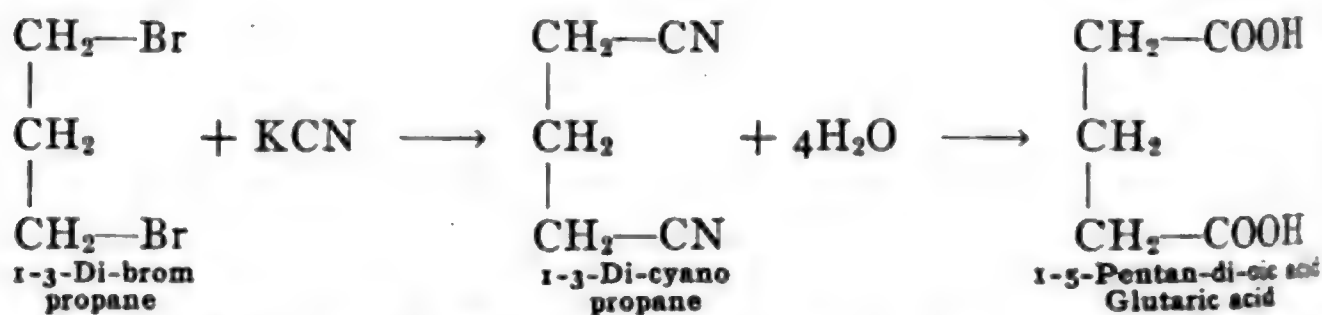
We began our study of the di-basic acids with oxalic acid which consists of two carboxyl groups *directly united*. We then took up malonic acid in which the two carboxyl groups are separated by *one* methylene group, and the homologues of this acid formed by substituting alkyl radicals into this methylene group. We considered next succinic acid in which the two carboxyl groups are separated by *two* methylene groups, and the homologues of it. We shall now consider di-basic acids in which the two carboxyl groups are separated by *more than two* methylene groups. Oxalic acid contains a *two carbon* straight chain, malonic acid a *three carbon* straight chain and succinic acid a *four carbon* straight chain. Therefore, our next acid to be considered must contain a *five carbon straight chain*, i.e., it must be derived from *pentane* and will be a **pentan-di-oic acid**. As succinic acid is structurally isomeric with mono-methyl malonic acid (iso-succinic acid) so mono-methyl succinic acid has an isomeric compound of exactly the same nature.



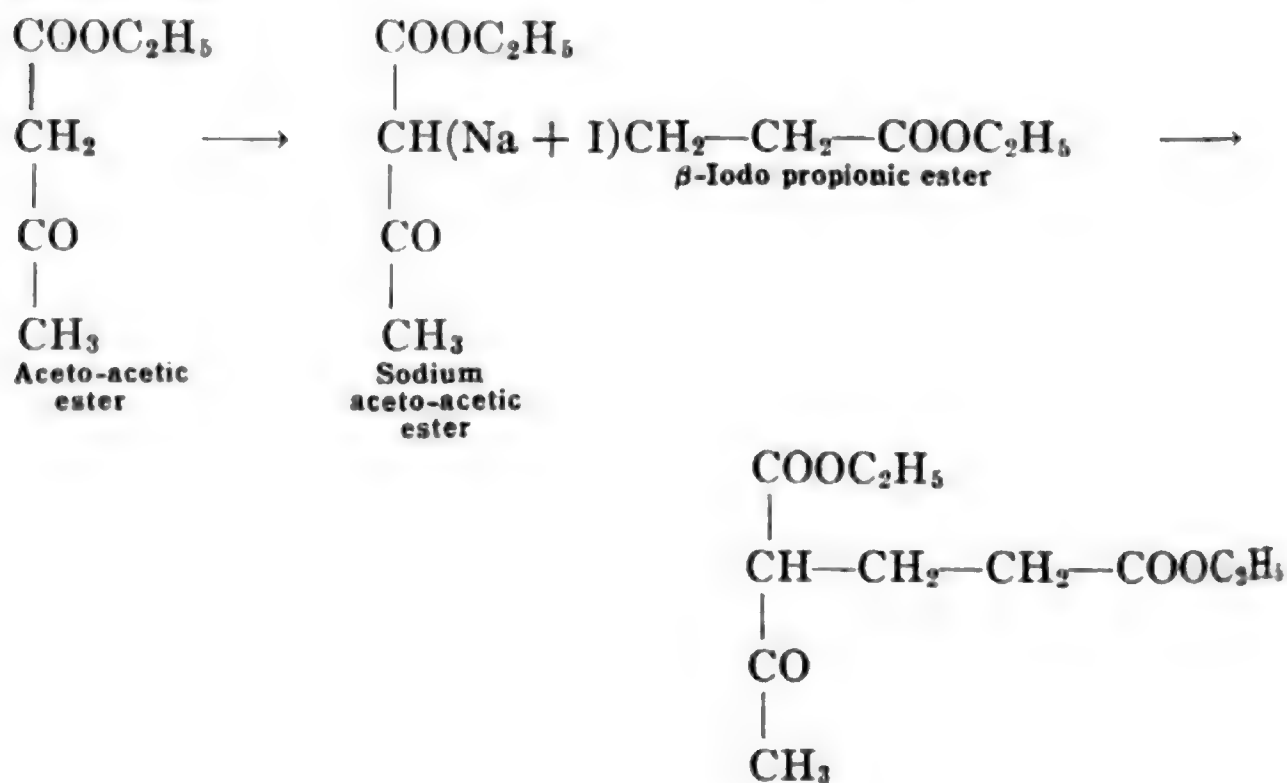
The isomerism in both of the above cases is like that between branched chain and straight chain compounds. In one compound a methyl group is substituted for a hydrogen atom in the intervening methylene group, thus making a branched chain. In the isomeric compound a new methylene group is interposed between the carboxyl groups, the compound being derived from a straight chain hydrocarbon. For this reason the methyl malonic acid could be called **iso-butan-di-oic acid** and succinic acid would be **normal butan-di-oic acid**.

This new acid, isomeric with mono-methyl succinic acid, pyro-tartaric acid, is known as **glutaric acid**, or systematically, as **1-5-pentan-di-oic acid**.

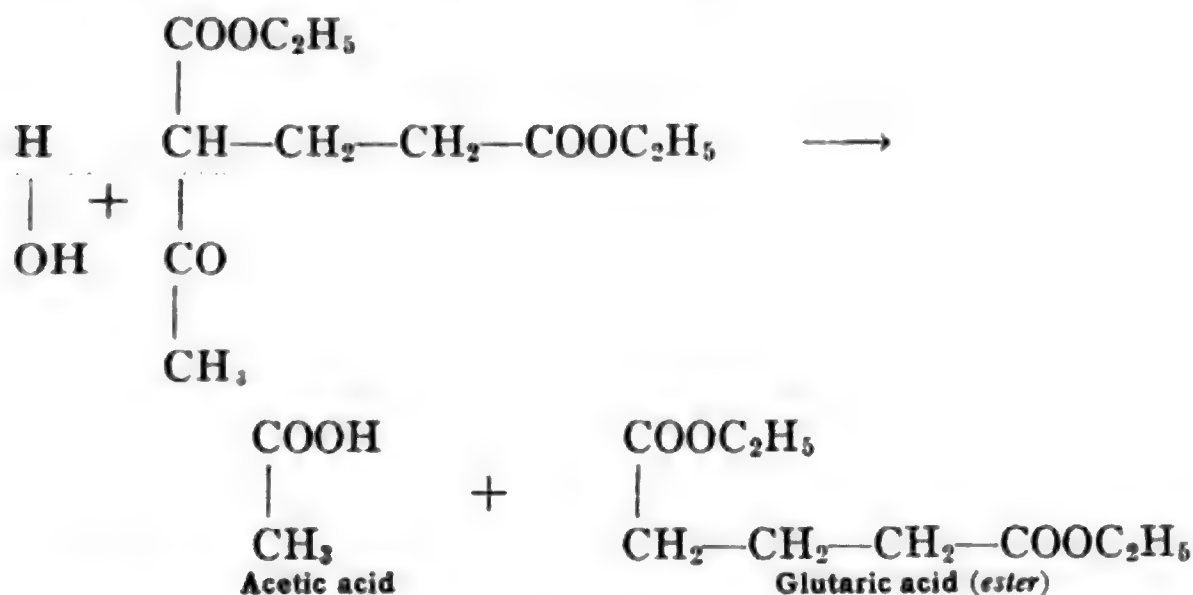
Synthesis from Propane.—The constitution of glutaric acid as 1-5-pentan-di-oic acid is proven by its synthesis from **1-3-di-cyano propane** which in turn is prepared from **1-3-di-brom propane**, as follows:



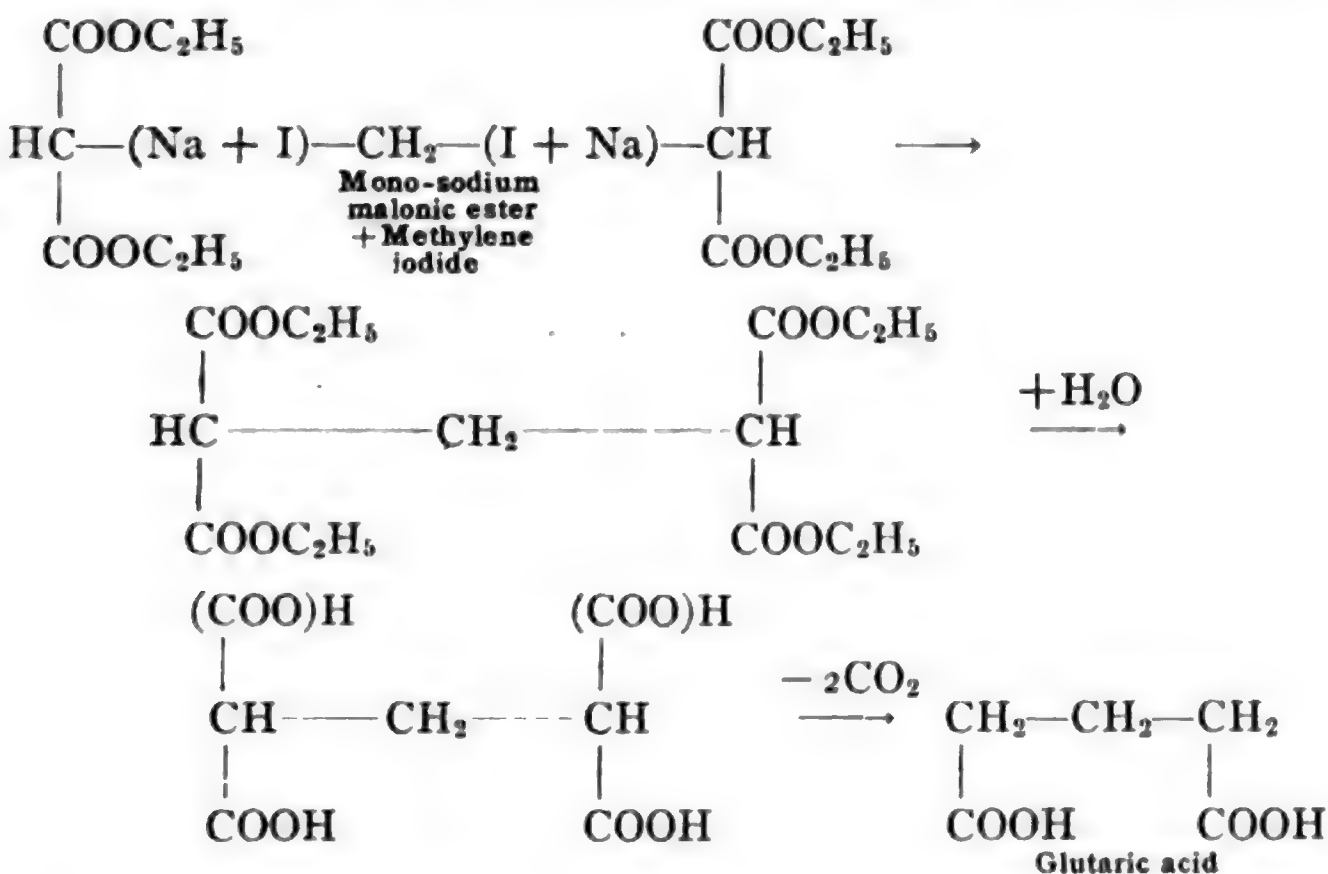
From Aceto-acetic Ester.—Glutaric acid may also be made by either the *aceto-acetic ester synthesis* or by the *malonic ester synthesis*, as follows,



The last product is then decomposed by the *acid hydrolysis* (p. 257) yielding **acetic acid** and **glutaric acid**.

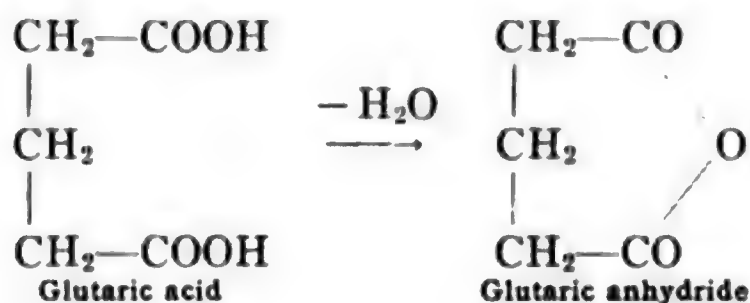


From Malonic Ester.—By the *malonic ester synthesis* it results from the condensation of two molecules of the malonic ester with **di-iodo methane**, **methylene iodide**, or with **form-aldehyde**, and the subsequent loss of carbon di-oxide from the condensation product, as follows:



Glutaric Anhydride.—These two syntheses show the wonderful adaptability of the aceto-acetic ester and the malonic ester syntheses in

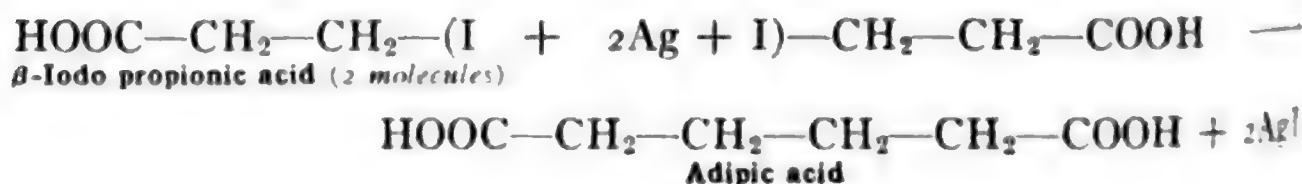
the preparation of organic compounds. **Glutaric acid** crystallizes in prisms which melt at 97.5° . It may be distilled at 290° but when heated slowly it forms an *inner anhydride* similar to that formed in the case of succinic acid.



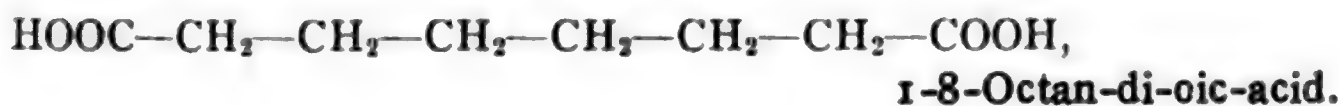
As explained when we were discussing the formation of anhydrides in connection with succinic acid, this anhydride of glutaric acid is still more easily formed because the two hydroxyl groups of the carboxyls at the end of a five carbon chain are very close together in space when we consider their space relations according to the tetra-hedral theory. Glutaric acid forms *esters* and also an *imide* analogous to those formed in the case of succinic acid. It is found in sugar beet juice and a derivative of it, viz., **glutaminic acid**, or α -**amino glutaric acid**, $\text{COOH—CH(NH}_2\text{)—CH}_2\text{—CH}_2\text{—COOH}$ (p. 391), is obtained as one of the hydrolytic products of **proteins**. This last is the chief source of the acid. The homologues of glutaric acid are analogous to those of succinic acid.

Higher Di-basic Acids

Adipic Acid—Of the di-carboxy acids which contain more than three carbon groups between the two carboxyls we need only mention two. **Adipic acid**, like glutaric acid, is found in the juice of the sugar beet. Its systematic name is **1-6 hexan-di-oic acid** and its formula is, $\text{HOOC—CH}_2\text{—CH}_2\text{—CH}_2\text{—CH}_2\text{—COOH}$. It may be synthesized by the same general methods as those described in connection with glutaric acid. The constitution of adipic acid has been proven by the following synthesis from β -**iodo propionic acid**, in which two molecules of the acid are condensed by means of silver.

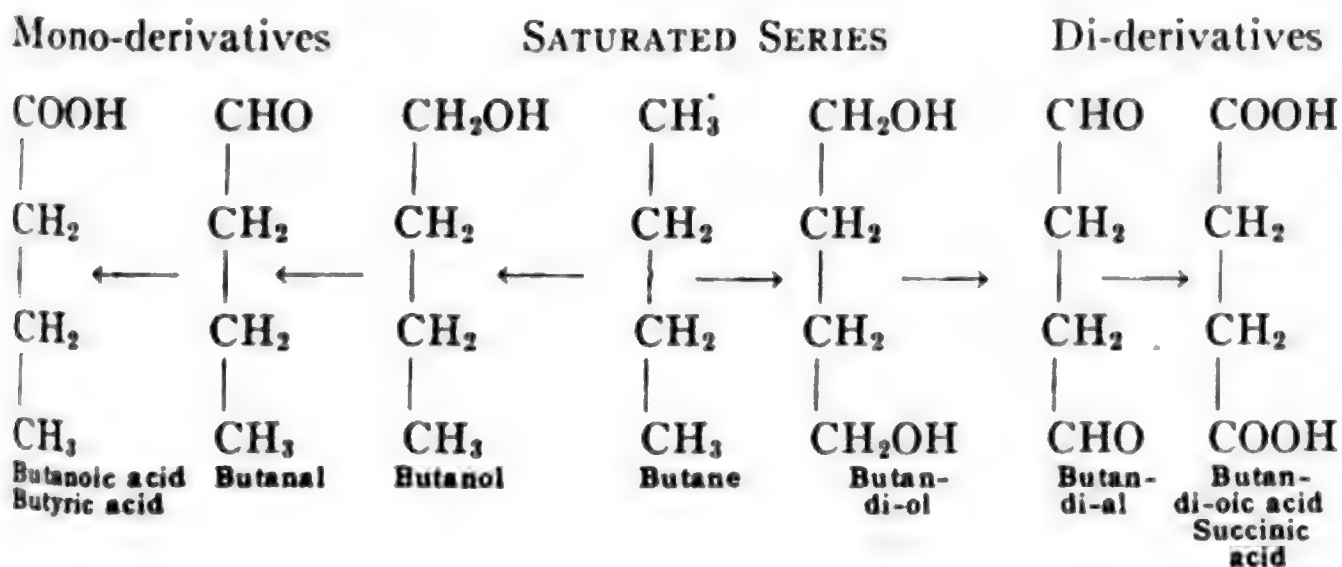


Suberic Acid.—The other di-basic acid which we shall simply mention is obtained as an oxidation product of *cork*. On this account it is known by the name of **suberic acid**. It has the composition, $C_8H_{14}O_4$, and it contains six methylene groups between the two carboxyl groups. The formula is

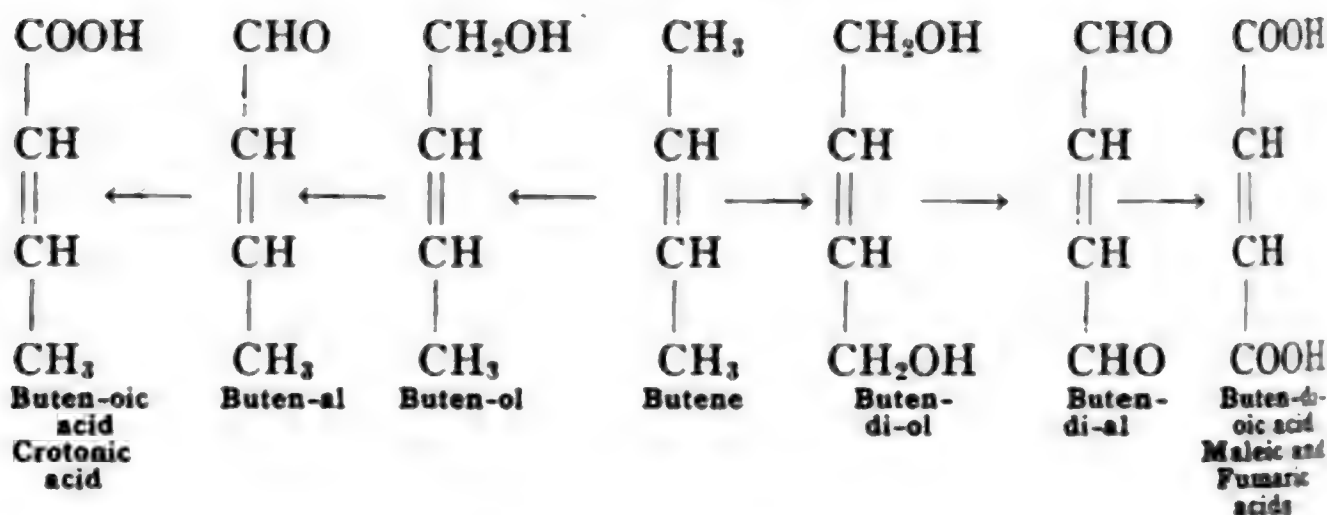


II. UNSATURATED DIBASIC ACIDS

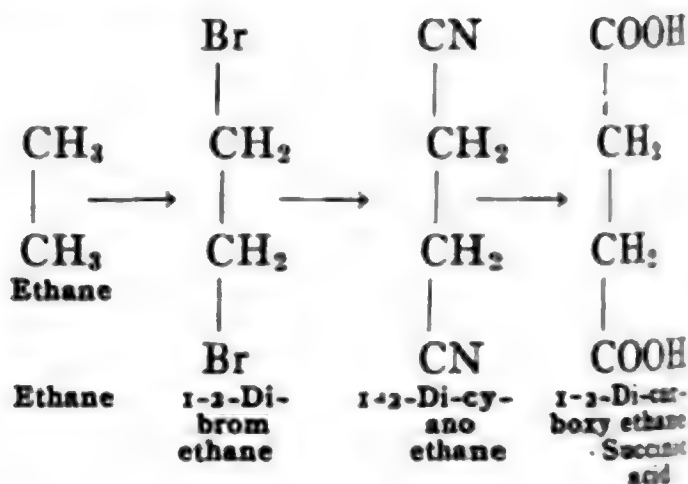
The *unsaturated dibasic acids* bear the same relation to the saturated dibasic acids, just considered, as the unsaturated mono-basic acids, **acrylic acid**, **crotonic acid**, etc. (p. 172), do to the saturated mono-basic acids, **acetic acid**, etc. They are also the oxidation products of the unsaturated hydrocarbons, alcohols, and aldehydes just as oxalic and succinic acids are of the corresponding saturated compounds. As the simplest dibasic acid containing an ethylene unsaturated group will contain two carboxyl groups and also two doubly linked carbon atoms there must be at least four carbons in the compound. This compound will therefore correspond to succinic acid of the saturated series. Now succinic acid may be derived from either **butane** by *oxidation* or from **ethane** by *substitution*. Similarly the corresponding unsaturated acid may be derived from *butene* by *oxidation* or from **ethene** by *substitution*. All of these general relationships may be represented as follows:



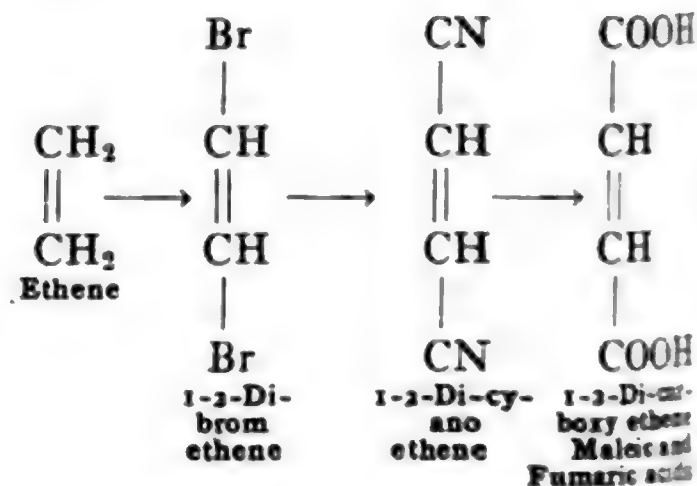
UNSATURATED SERIES



SATURATED SERIES



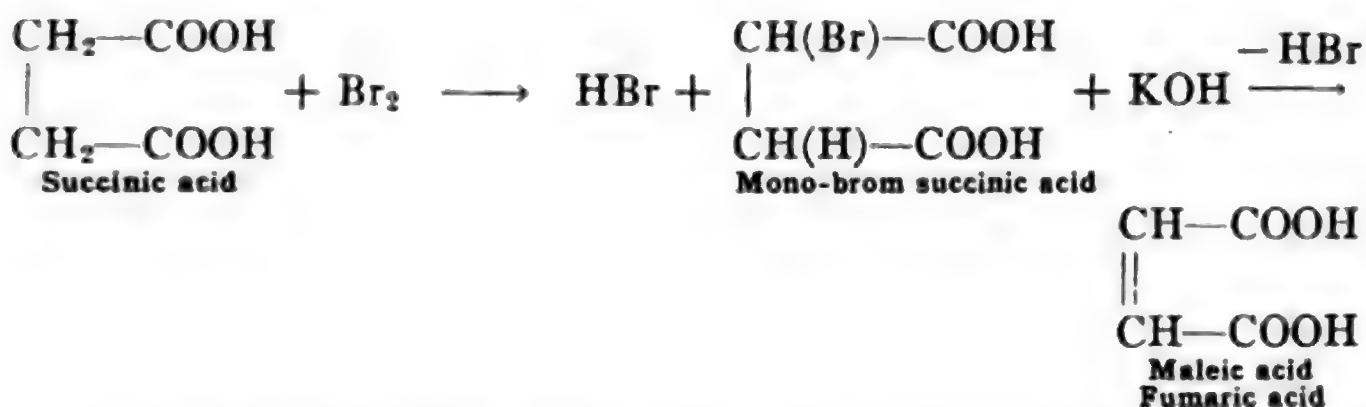
UNSATURATED SERIES



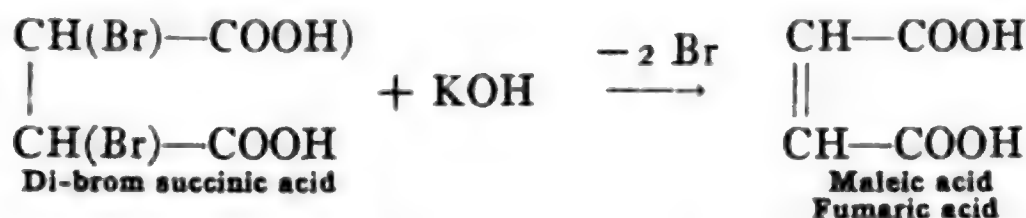
Maleic Acid $\text{HOOC}-\text{CH}=\text{CH}-\text{COOH}$ **Fumaric Acid**

Synthesis from Succinic Acid.—Two isomeric acids are known of the constitution of di-carboxy ethene, or *buten-di-oic acid*. They are named **maleic acid** and **fumaric acid**. Their synthesis from succinic acid establishes their constitution. **Mono-brom succinic acid** when

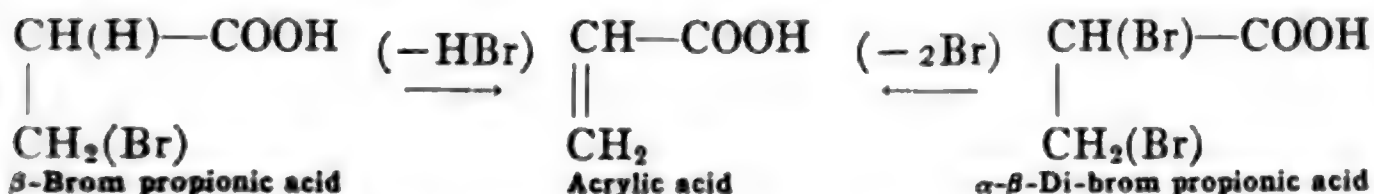
heated with potassium hydroxide, loses hydrogen bromide and yields maleic acid.



Also **di-brom succinic acid** loses two atoms of bromine and likewise yields maleic acid.

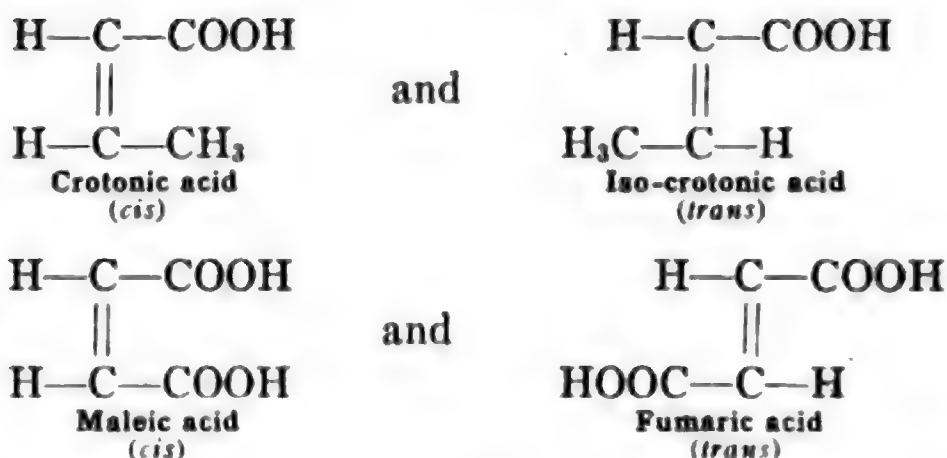


This synthesis is exactly analogous to the formation of the mono-basic unsaturated acid, acrylic acid, from *beta*-brom propionic acid, or from *alpha-beta*-di-brom propionic acid (p. 172).

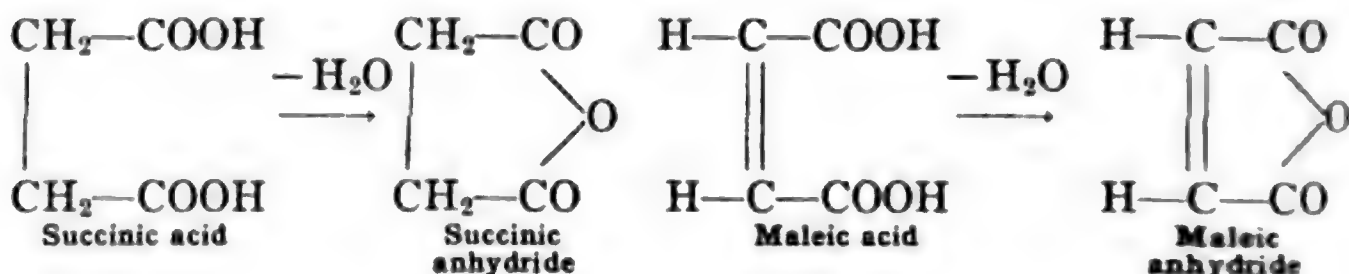


The reverse of these reactions: viz., the conversion of maleic and fumaric acids, by the addition of hydrogen bromide, into mono-brom succinic acid; by the addition of two bromine atoms, into di-brom succinic acid; and also by the addition of two hydrogen atoms, into succinic acid itself; all show these same relations of maleic and fumaric acids to succinic acid and its bromine substitution products and establish the constitution of these isomeric di-basic unsaturated acids as given. The two acids may also be prepared from malic acid which is, in fact, the chief method by which they are prepared. This reaction will be considered later when malic acid itself is studied.

Isomerism of Maleic and Fumaric Acids.—The isomerism of maleic and fumaric acids is *stereo-isomerism* of the *geometric type*. It is exactly like that of the two **crotonic acids** (p. 177).



The proof that maleic acid corresponds to the *cis* formula and fumaric acid to the *trans* formula is in the fact that **maleic acid** readily forms **an anhydride** while **fumaric acid** does *not*. If the two carboxyl groups are on the *same* side, as in the *cis* form, the compound would have a tendency to lose water easily; while if the two carboxyl groups are on *opposite* sides, as in the *trans* form, the compound would not have this tendency to lose water. The space relations of the two carboxyl groups is readily seen if the two compounds are built up by means of tetra-hedral models. It is analogous to that in succinic acid and glutaric acid (p. 281).



Conversion of Maleic Acid and Fumaric Acid into Each Other.—

The conversion of maleic and fumaric acids into each other is an exceedingly interesting and important relation. When fumaric acid is strongly heated above 200° no anhydride of fumaric acid is formed, as has been stated, but **maleic anhydride** is obtained. On the other hand, when maleic acid is heated above its melting point, or when it is heated under pressure to 130° , it is converted, little by little, into **fumaric acid**. Also, when maleic acid is treated with concentrated hydrochloric acid at 10° , or with hydrobromic acid at 0° , or boiled with hydriodic acid, it is likewise converted into **fumaric acid**. When maleic anhydride is distilled with phosphorus penta-chloride the di-chloride of fumaric acid, **fumaryl chloride**, results. These transformations show

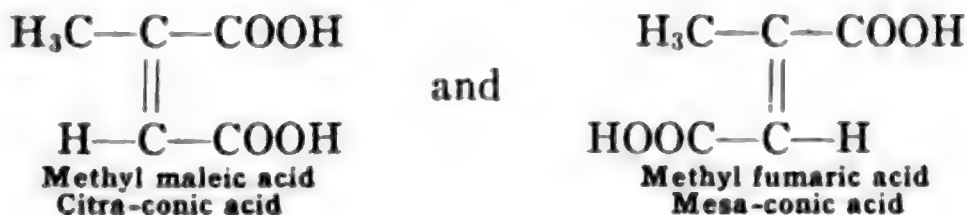
the close relation which the two acids bear to each other and will be readily seen to be dependent, probably, upon their *stereo-chemical* character. It will be out of place, in this study, to discuss more fully the processes by which these reciprocal transformations are effected. For these discussions the student is referred to such books as **Cohen**, and **Meyer and Jacobson**.

Maleic acid crystallizes in rhombic prisms which melt at 130° and begin to boil and lose water forming the anhydride at 160° . The acid is easily soluble in water. The anhydride crystallizes in thin prisms which melt at 53° and boil at 202° . The chief method of obtaining maleic acid, as has been said, is by heating malic acid. This has given to the acid its name of maleic.

Fumaric acid occurs naturally in many plants, especially in *Fumaria vulgaris*, from which it derives its name. It is also found in some fungi. From concentrated solution it crystallizes in fine needles. When heated to 200° it volatilizes and at higher temperatures is transformed into maleic anhydride. It is difficultly soluble in water.

Citra-conic, Mesa-conic and Ita-conic Acids

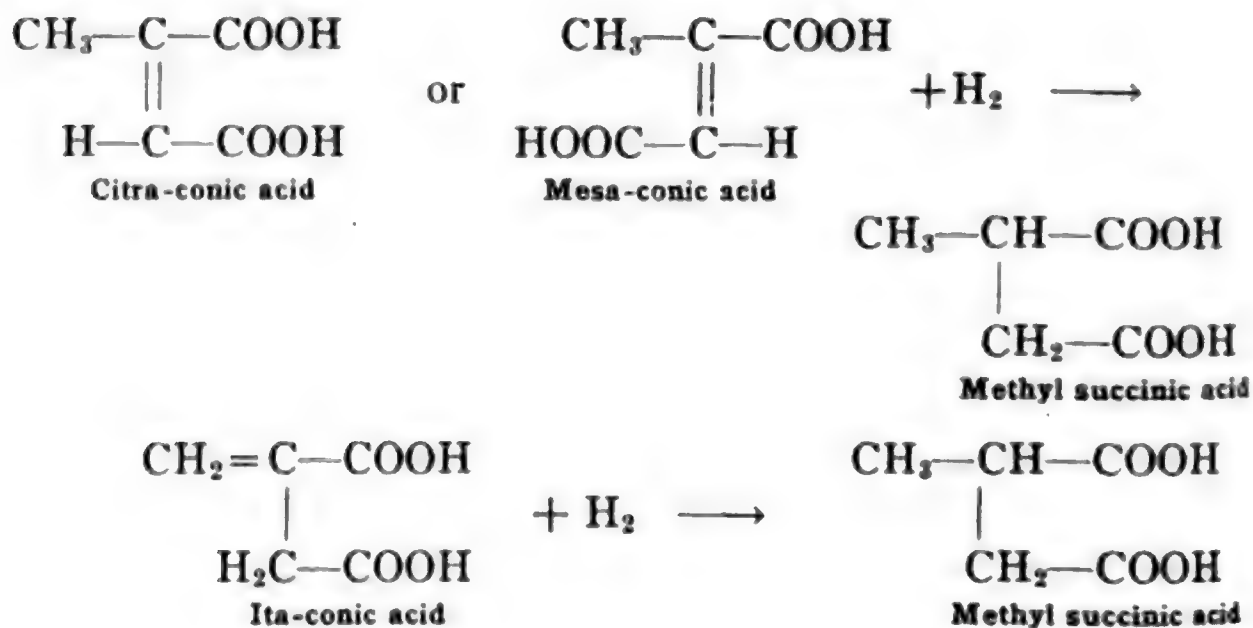
The only homologous unsaturated di-basic acids which we shall consider are those formed by substituting methyl for one of the non-hydroxy hydrogen atoms, in maleic acid and in fumaric acid. Plainly each of these two acids should yield a methyl substitution product and those two products should differ from each other just as the maleic and fumaric acids differ, *i.e.*, they should be *geometric isomers*. The formulas, corresponding to those of maleic and fumaric acids, are



Citra-conic and Mesa-conic Acids.—Two such geometrically isomeric acids are known to which the names **citra-conic acid** and **mesa-conic acid** have been given. **Citra-conic acid** melts at 80° and easily yields an anhydride. It must, therefore, be represented by the *cis* formula and is the methyl derivative of maleic acid. **Mesa-conic acid** melts at 202° and does not yield an anhydride. It should, therefore, be

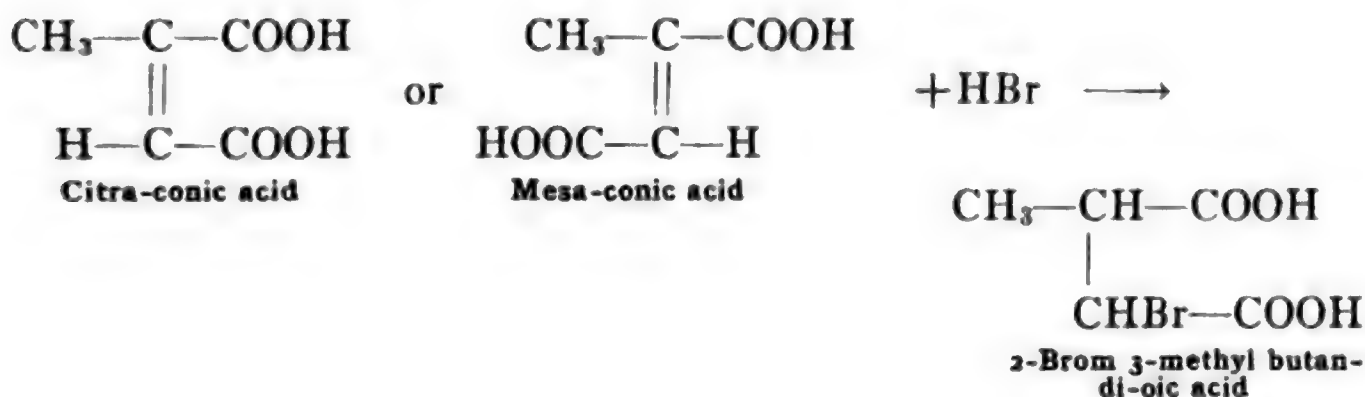
represented by the *trans* formula and is the methyl derivative of fumaric acid. The two acids are obtained from **citric acid** which we shall study later, and from which the former derives its name. Citra-conic acid and mesa-conic acid are reciprocally transformed into each other as in the case of maleic and fumaric acids. By the addition of hydrogen they are each converted into the corresponding saturated acid, viz., **methyl succinic** or **pyrotartaric acid**. By the addition of hydrobromic acid they each yield **methyl brom succinic acid**, **2-brom 3-methyl butan-di-oic acid**, and the addition of bromine converts them each into **methyl di-brom succinic acid**, **2-methyl 2-3-di-brom butan-di-oic acid**. Thus their relationship to succinic acid and to maleic and fumaric acids is fully established and their constitution proven.

Ita-conic Acid.—There is, however, a *third* acid known of the same composition as the two preceding. It is called **ita-conic acid** and like the others is obtained from citric acid by distillation. More than the two isomers just explained are not possible according to geometric isomerism. The isomerism, therefore, of this new acid with the other two must be explained in some other way and has been shown to be structural isomerism due to the different position of the double bond. We have spoken of the fact that both citra-conic and mesa-conic acids, by the addition of hydrogen, are converted into methyl succinic acid. This same result is obtained with ita-conic acid also as may be explained by the following reactions,

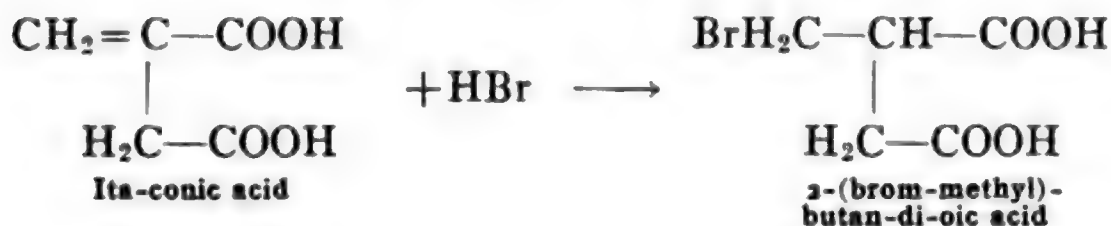


In this case the products are all the *same* but if hydro-bromic acid or bromine is added the products are *different* in the case of ita-conic

acid. Citra-conic and mesa-conic acids with hydrobromic acid yield, *2-brom 3-methyl butan-di-oic acid*,



Ita-conic acid, however, yields *2-(brom-methyl) butan-di-oic acid*.



The constitution of **ita-conic acid** as **methylene succinic acid** is thus established. Di-basic acids which contain a triple bond and, therefore, related to propin-oic acid are known but will not be considered.

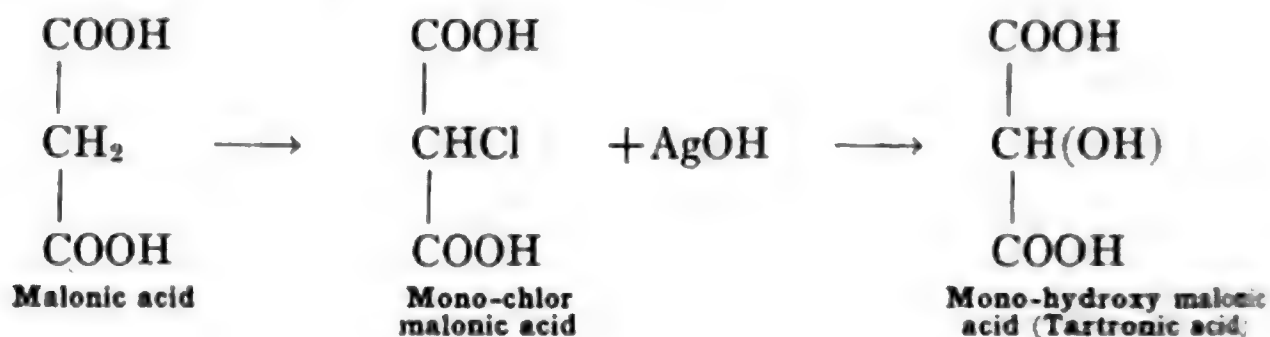
III. HYDROXY DI-BASIC ACIDS

We come now to the study of the substituted di-basic acids. Of the compounds derived from the di-basic acids by substitution in the carbon-hydrogen groups, only those obtained by substituting the *hydroxyl* group will be considered at this time. The corresponding *amino* substitution products are of importance but they will be considered later together with amino acids derived from the mono-basic acids. The other classes of substitution products, *e.g.*, *halogen*, *cyanogen*, etc., are not of importance by themselves but will be taken up in connection with compounds to which they are directly related. As oxalic acid, the first di-basic acid which we considered, has no carbon group other than carboxyl, it is impossible to obtain from it a substitution product. Therefore, the first di-basic acid to yield substitution products is malonic acid.

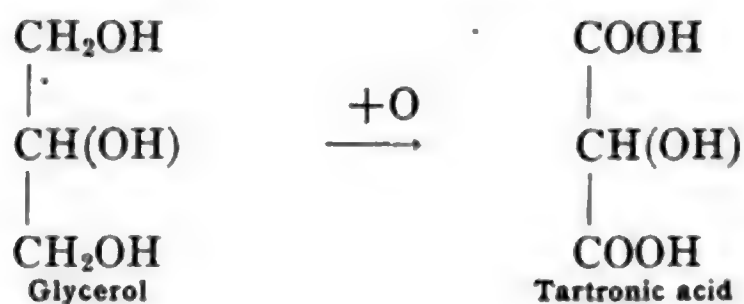
HYDROXY MALONIC ACIDS

Tartronic Acid $\text{HOOC}-\text{CH}(\text{OH})-\text{COOH}$ **Mono-hydroxy Malonic Acid**

Synthesis from Malonic Acid.—Tartronic Acid is obtained from malonic acid directly through mono-chlor malonic acid,

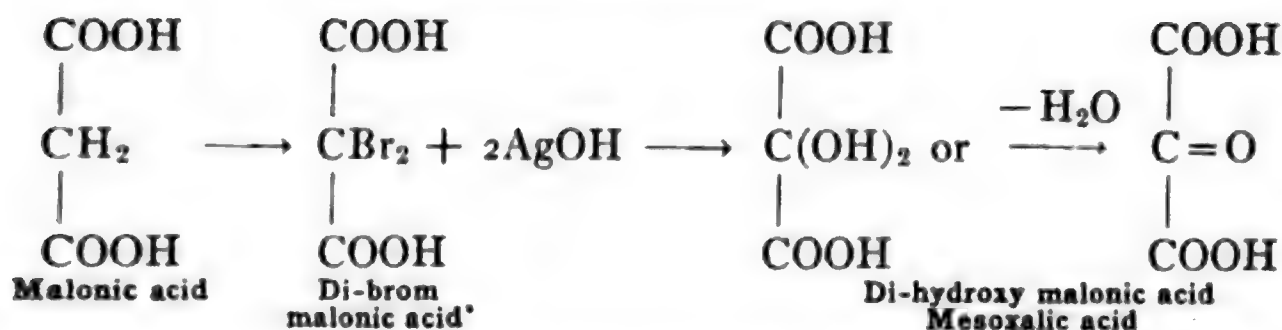


From Glycerol.—This synthesis shows tartronic acid to have the constitution given, *i.e.*, **mono-hydroxy malonic acid**. It may also be obtained from glycerol by oxidation. In this reaction the two primary alcohol groups in glycerol are both oxidized to carboxyl while the secondary alcohol group remains unchanged.

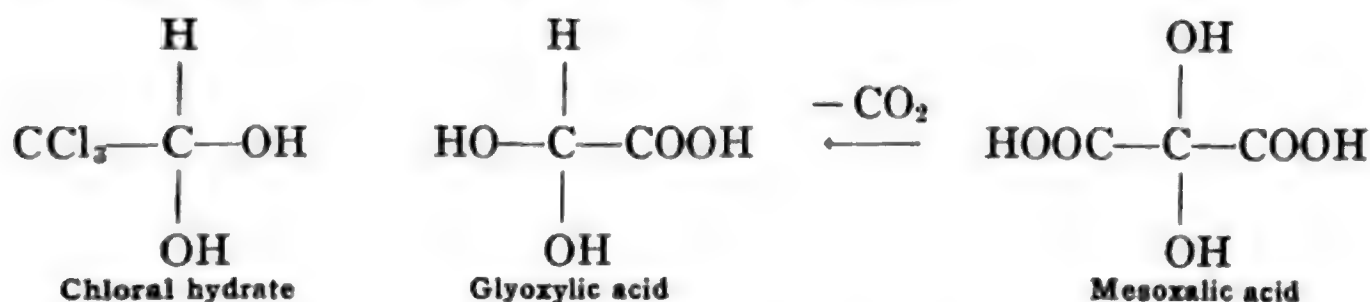


Mesoxalic Acid $\text{HOOC}-\text{C}(\text{OH})_2-\text{COOH}$ **Di-hydroxy Malonic Acid**

We have often referred to the fact that two hydroxyl groups linked to the same carbon yield compounds that are unstable and which by loss of water are converted into other compounds which are stable. In the case of the hydroxyl derivatives of malonic acid we have an exception to this rule, for di-brom malonic acid yields with silver hydroxide a compound which probably has the formula of a *di-hydroxy malonic acid*. As such substituted hydroxyl groups must, in malonic acid, be united to the same carbon atom, and the compound formed is a stable one, we either have an exception to the above given general rule or we must explain the constitution of the resulting compound in some other way.



According to one formula mesoxalic acid has the constitution of a normal di-hydroxy malonic acid contrary to what we should expect. According to the second formula it is a *ketone acid*, an anhydride of the first. It should be recalled here that in connection with glyoxylic acid (p. 252) we emphasized the fact that in **chloral hydrate** (p. 226) and in **glyoxylic acid** we have a carbon atom linked to a strongly negative group, viz., ($-\text{CCl}_3$) or ($-\text{COOH}$). In **mesoxalic acid** the same condition is present only in this case it is doubled.

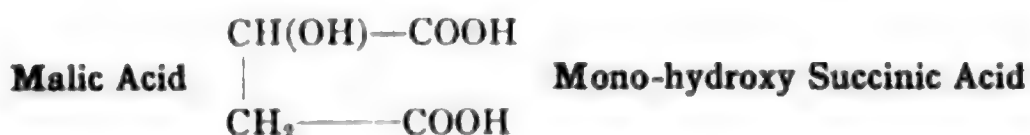


Under such conditions two hydroxyl groups may be linked to this carbon forming a stable compound. Also mesoxalic acid by loss of (CO_2) by heat yields glyoxylic acid, as above.

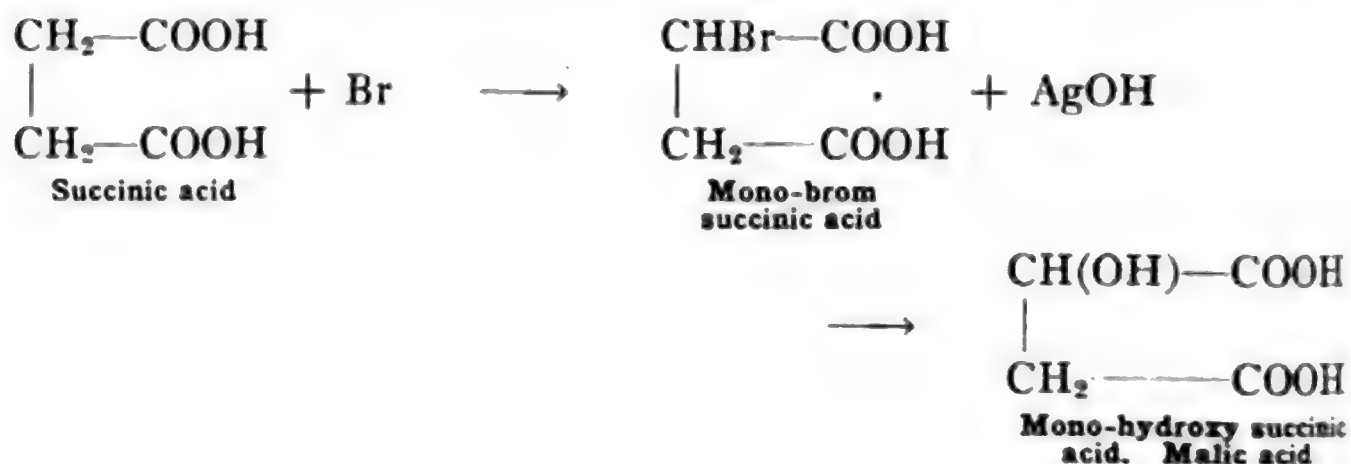
It should be stated that the evidence is not complete and the constitution of mesoxalic acid is generally accepted as not yet established.

HYDROXY SUCCINIC ACIDS

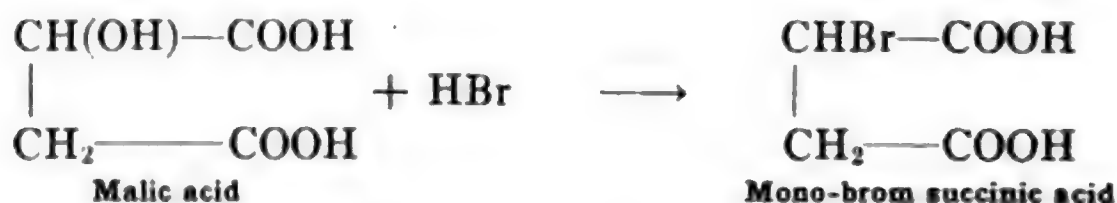
The other hydroxy di-basic acids which we shall consider are the hydroxyl substitution products of succinic acid. These hydroxy succinic acids are commonly occurring substances and, both from the standpoint of theory and of practical value, are most important compounds. The *mono-hydroxy* succinic acid is commonly known as **malic acid**, and the *di-hydroxy* compound is the common substance, **tartaric acid**.



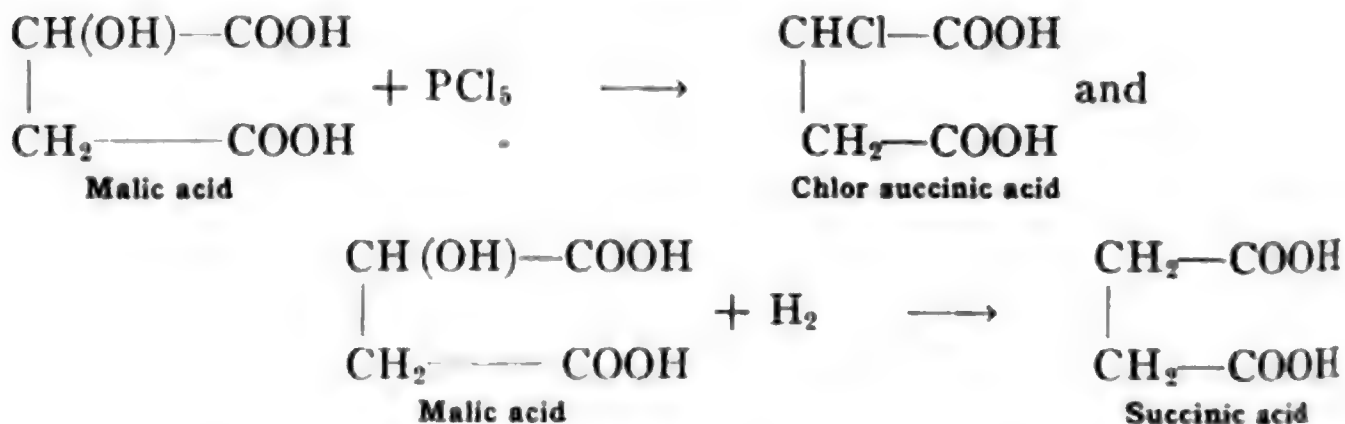
Relation to Succinic Acid.—The constitution of malic acid is fully established by its relation to succinic acid. It may be synthesized from mono-brom succinic acid by treatment with silver hydroxide.



The reverse of this reaction takes place when malic acid is heated with hydrobromic acid, *i.e.*, malic acid is thus converted into mono-brom succinic acid.

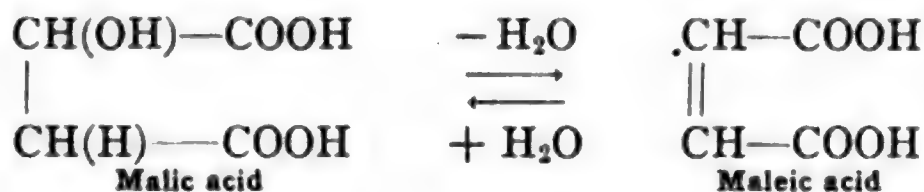


When malic acid is warmed with phosphorus penta-chloride it yields chlor succinic acid, and when reduced by means of hydrogen iodide, hydrogen is added and succinic acid results.



Relation to Maleic and Fumaric Acids.—The constitution of malic acid is also proven by its relation to maleic and fumaric acids. It was mentioned, under maleic acid, that this acid received its name from the fact that it was obtained by heating malic acid. The reac-

tion consists in the loss of a molecule of water from the malic acid. The reverse reaction may also be accomplished by heating maleic or fumaric acids in a sealed tube with water. The two reactions are as follows:

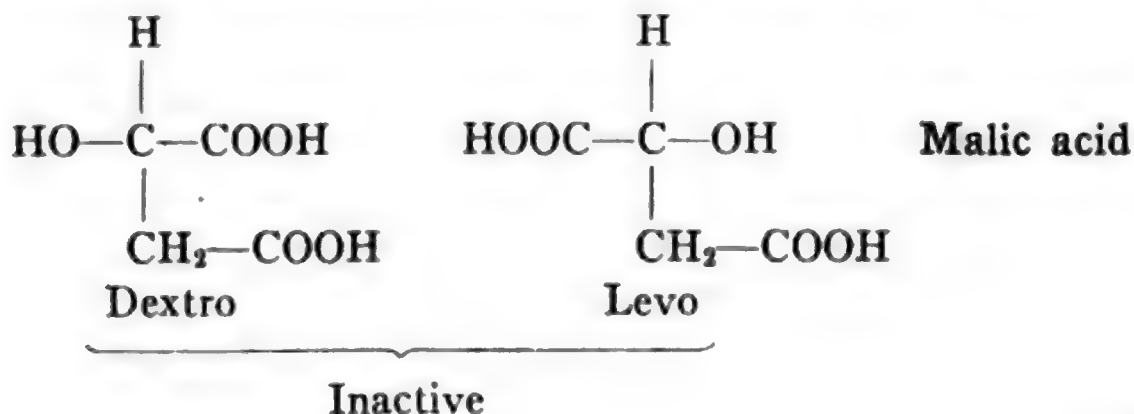


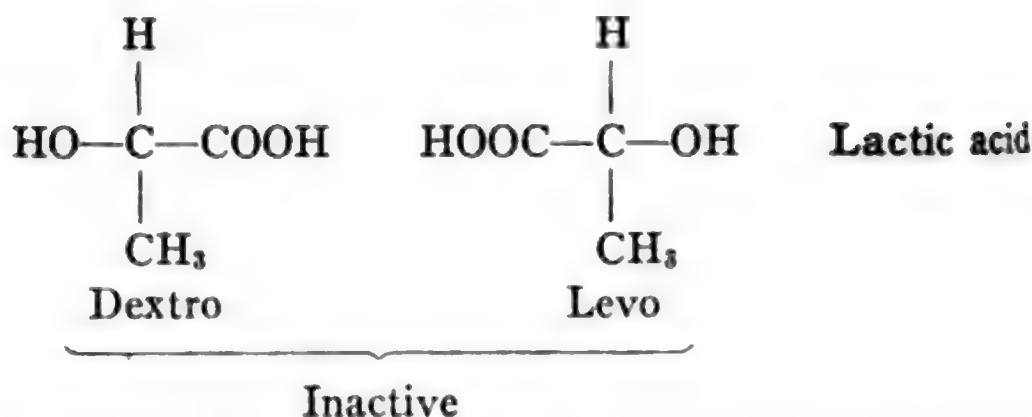
The loss of water from hydroxy acids and the formation of unsaturated acids has been met with before in connection with the *beta*-hydroxy mono-basic acids, e.g., **hydracrylic acid**, **β -hydroxy propionic acid**, and its conversion into **acrylic acid**, *propenoic acid* (p. 172). In such cases the *beta*-hydroxy acid loses water from two neighboring carbon groups thereby creating a double bond.



In malic acid the hydroxyl group is in the *beta*-position in relation to one of the carboxyl groups and the formation of an unsaturated acid by the loss of water would be expected.

Stereo Isomerism of Malic Acid.—On examination of the formula of malic acid it will be seen that one of the carbons is *asymmetric*, i.e., it has united to it four different elements or groups, viz., (—H), (—OH), (—COOH), and (—CH₂—COOH). We should, therefore, expect to find that malic acid is optically active and that it exists in the three forms of *dextro*, *levo*, and *inactive*. This is in accordance with the facts. The formulas for the three stereo-isomeric forms of malic acid may be written as follows, corresponding exactly to those for lactic acid.



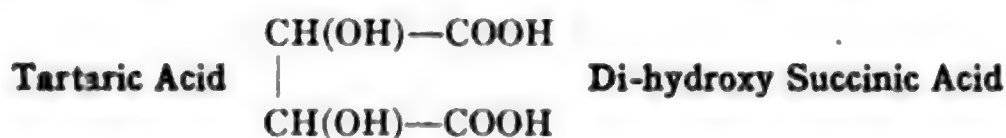


The study of malic acid in connection with its stereo-isomerism, together with the similar study of the related acids, lactic, tartaric, maleic and fumaric has been of the greatest importance in establishing our ideas of stereo-isomerism.

Active Malic Acid.—Malic acid occurs widely distributed in nature. It is found partly free and partly combined, in unripe apples, from which it derives its name, in unripe mountain ash berries, in cherries, grapes, goose-berries, quinces and other fruits. It is found as the calcium salt in sumach berries, in tobacco leaves and in maple sap from which it separates as a fine crystalline sediment obtained when the syrup is filtered. The free acid crystallizes in tufts of glistening deliquescent needles which melt at 100° . When heated to 120° – 130° it loses water and is converted into maleic and fumaric acids. It is easily soluble in water or in alcohol. The natural malic acid, in crystalline form, or in concentrated solution, is dextro rotatory. The optical rotation, however, *changes with the concentration* of the solution. In dilute solution, up to 34 per cent., at 20° , it is levo rotatory. At this concentration it becomes inactive but if the concentration is increased it becomes dextro rotatory. In solution in acetone malic acid is levo rotatory. When levo malic acid is treated with phosphorus penta-chloride, according to the reaction previously given, chlor succinic acid is obtained, but it is the dextro form which results, and when this dextro chlor succinic acid is converted back into malic acid, by means of silver hydroxide, we obtain dextro malic acid. Thus we have a means of converting the levo into the dextro form. Also, if dextro malic acid is acidified with sulphuric acid levo malic acid is formed. We may also obtain the dextro malic acid by the reduction of dextro tartaric acid, as we shall see later.

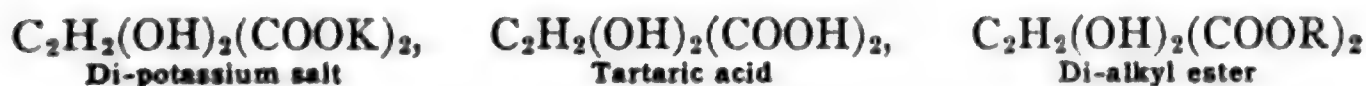
Inactive Malic Acid.—When malic acid is prepared *synthetically*, from inactive compounds, we obtain the *inactive* malic acid. Thus,

inactive bromsuccinic acid, inactive amino succinic acid and inactive tartaric acid, (racemic acid), all yield the inactive form of malic acid. Also, by the reaction previously given, by heating maleic acid in a sealed tube with water, inactive malic acid results. The inactive malic acid may be split into its optical components by proper reactions as was discussed under lactic acid and as will be again mentioned in connection with tartaric acid. Inactive malic acid crystallizes easily, is not deliquescent and is less soluble than ordinary active malic acid.



By the introduction of one more hydroxyl group into malic acid we obtain a *di-hydroxy* succinic acid which, as a di-hydroxy compound, is analogous to mesoxalic acid and bears the same relation to succinic acid and to malic acid that mesoxalic acid bears to malonic acid and to tartronic acid. The acid of this constitution is the commonly occurring substance **tartaric acid**. That tartaric acid contains *two carboxyl groups* and at the same time *two alcohol hydroxyl groups* and that it is in fact **di-hydroxy succinic acid** is proven by several syntheses and reactions.

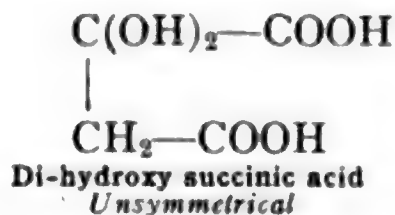
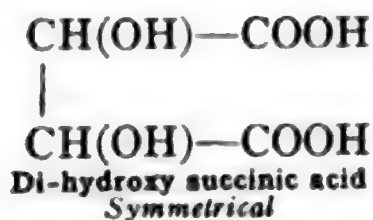
Di-basic and Di-alcoholic.—That tartaric acid is di-basic, *i.e.*, that it contains two carboxyl groups is shown by the fact that it forms *di-alkyl esters* and *di-metal salts*.



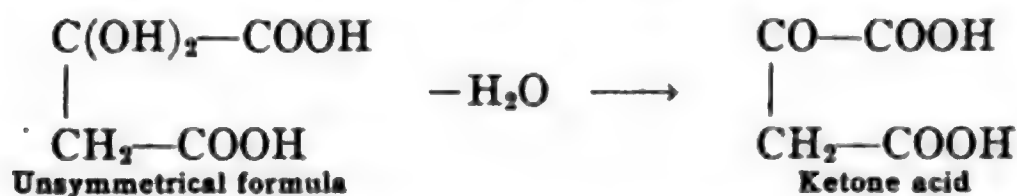
That it contains two alcohol hydroxyl groups is proven by the fact that its di-alkyl esters form *di-acetyl derivatives*,



Symmetrical.—Two formulas are, however, possible for a di-hydroxy succinic acid, viz., the *symmetrical* and the *unsymmetrical*.

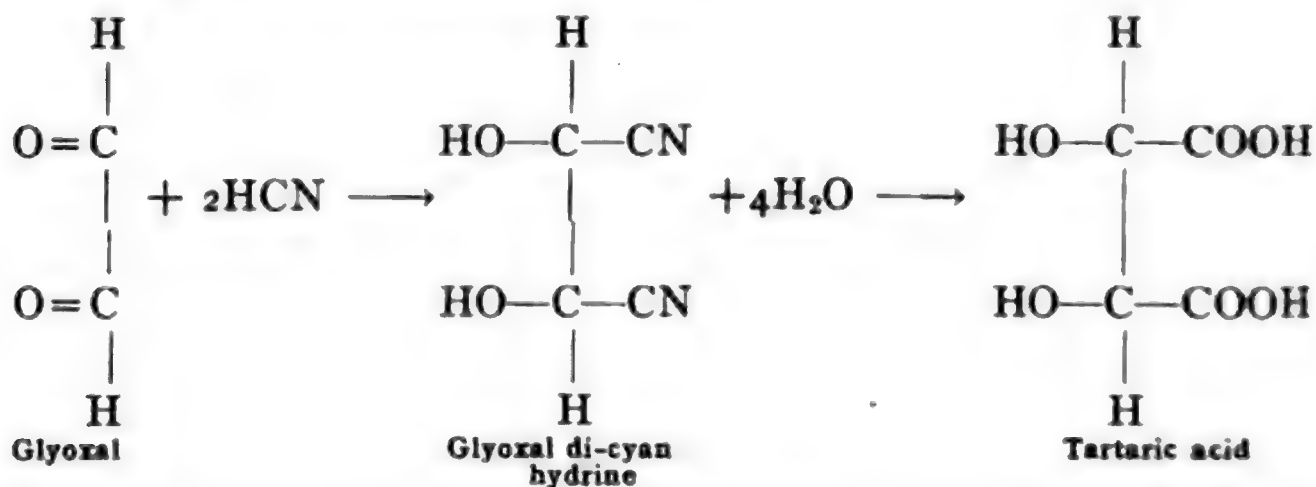


That tartaric acid is not the unsymmetrical di-hydroxy succinic acid is shown by the fact that an acid of this constitution would, by loss of water, yield a ketone acid, as follows:



Such an acid as this ketone acid is known and is called **oxal acetic acid**, and tartaric acid does not yield this acid on heating nor does it show any properties of a ketone acid. We, thus, have no evidence that tartaric acid is the unsymmetrical di-hydroxy succinic acid. That tartaric acid is, in fact, the *symmetrical* di-hydroxy succinic acid is proven by its synthesis from **glyoxal**, and also by its synthesis from **succinic acid** itself.

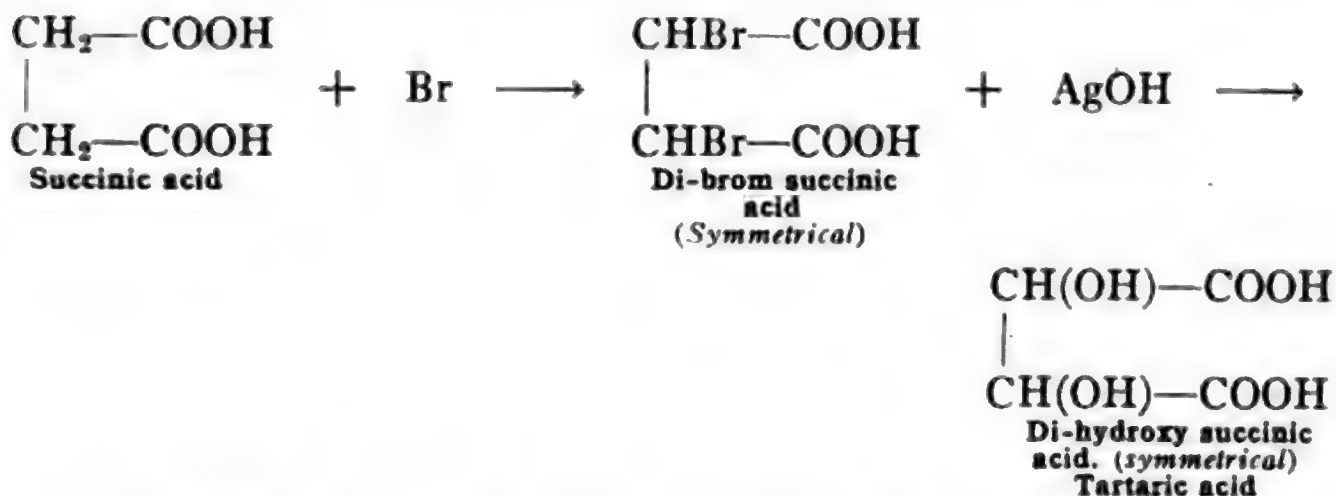
Synthesis from Glyoxal.—Glyoxal, being a *di-aldehyde*, (p. 261), forms a *di-addition product* with hydrogen cyanide, HCN, and this di-cyanide addition product hydrolyzes and yields tartaric acid. The reaction may be expressed as follows,



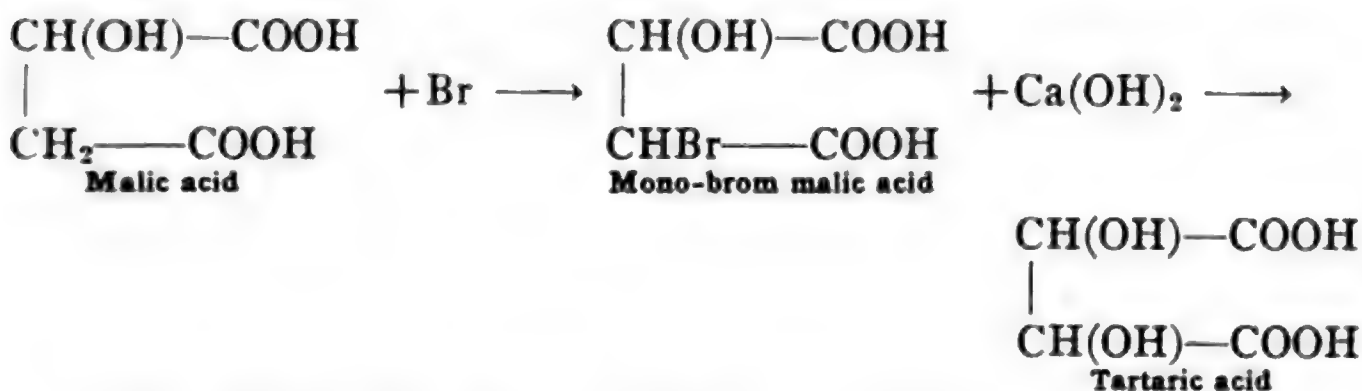
According to this synthesis tartaric acid must have the two hydroxyl groups linked to *different* carbon atoms, and also the two carboxyl groups must likewise be linked to *different* carbon atoms and furthermore each carbon of the original glyoxal must have *one hydroxyl* group, *one carboxyl* group and *one hydrogen* atom linked to it. It must therefore be the symmetrical compound.

From Succinic Acid.—The synthesis of tartaric acid from succinic acid also proves that it must be the symmetrical di-hydroxy succinic acid. When succinic acid, by means of bromine, yields the symmetrical di-brom succinic acid this, in turn, when treated with silver hydroxide,

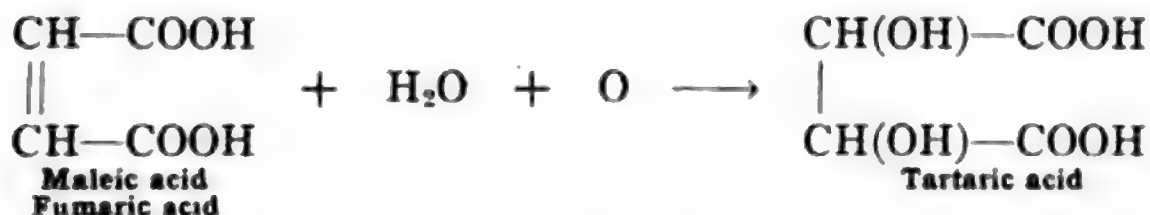
has the two bromine atoms replaced by two hydroxyl groups, and tartaric acid results,



From Malic Acid.—Another synthesis of tartaric acid is from malic acid. When malic acid is treated with bromine it yields a mono-brom malic acid which by means of calcium hydroxide yields tartaric acid.

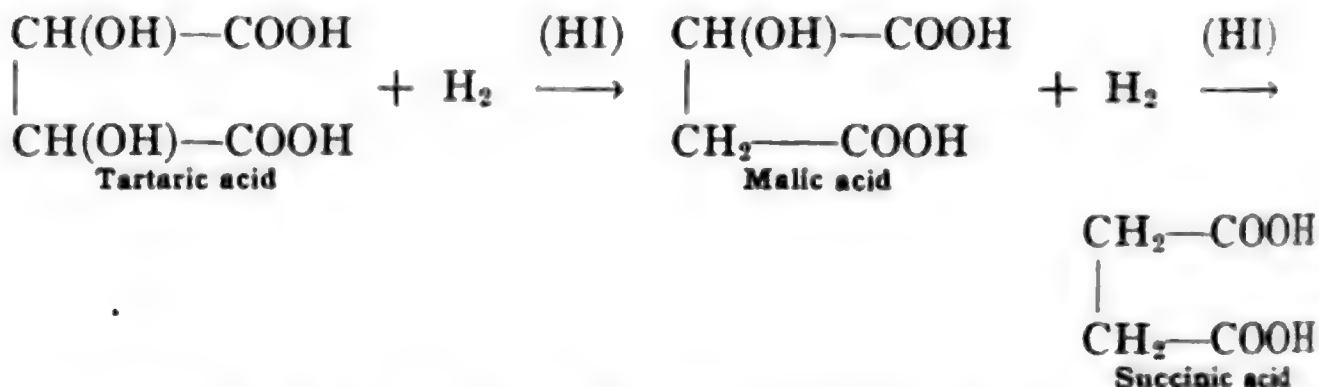


From Maleic and Fumaric Acids.—Still another synthesis is from maleic and fumaric acids. When these acids are cautiously oxidized by means of potassium permanganate or chameleon solution water and oxygen are added to the unsaturated acids and the product is tartaric acid.

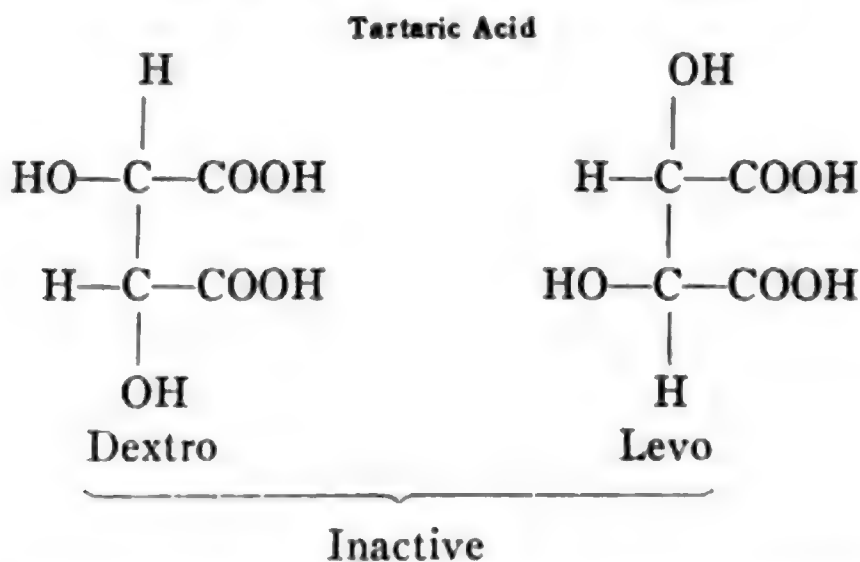


Reduction to Malic and Succinic Acids.—The relation of tartaric acid to malic acid and to succinic acid is shown, also, by the conversion of tartaric acid into each of these acids successively, which is, in fact, more easily accomplished than the reverse reactions just described.

By reduction with hydrogen iodide, tartaric acid yields, first, malic acid, and then succinic acid,



Isomerism of Tartaric Acid.—Examination of the formula for tartaric acid, which, by the facts given above, has its constitution fully established as **symmetrical di-hydroxy succinic acid**, shows the interesting fact that there are present *two asymmetric carbon atoms*, and that each of these has linked to it the *same set of four different groups*. We should, therefore, expect to find tartaric acid existing in the *dextro*, the *levo* and the *inactive* forms. The stereo-chemical formulas similar to those of lactic and malic acids we may write as follows,



One of the above formulas may be taken to represent the dextro form and the other the levo. The mixture of the two will produce the inactive acid. Now these three forms of tartaric acid are all known and they bear to each other exactly the same relation as has been explained in connection with lactic acid. The inactive form is able to be split into its two optical components like the inactive lactic acid. These three acids are as follows,

Dextro Tartaric Acid.—The ordinary tartaric acid as it occurs in grapes.

Levo Tartaric Acid.—Obtained from the inactive form, by splitting it into its optical isomers.

Racemic Acid (inactive).—Also found in grapes and able to be split into its active isomers.

However, a *fourth* form of tartaric acid is known, viz.,

Meso-tartaric Acid.—Also inactive but unlike racemic acid it cannot be split into active isomers.

It is this fourth unresolvable inactive tartaric acid which gives to tartaric acid its especial interest and importance in connection with the theory of stereo-isomerism. This acid, like the other three, has been fully explained in accordance with the tetra-hedral theory of **van't Hoff** and **LeBel**. The explanation rests upon the fact that there is a *second asymmetric carbon atom* in tartaric acid. We may construct, by models, or, by drawings, space-formulas for tartaric acid. According to the tetra-hedral theory, the dextro, levo and racemic inactive forms will be as follows, analogous to the corresponding formulas for the three lactic acids. The meso-tartaric acid is represented by the third drawing.

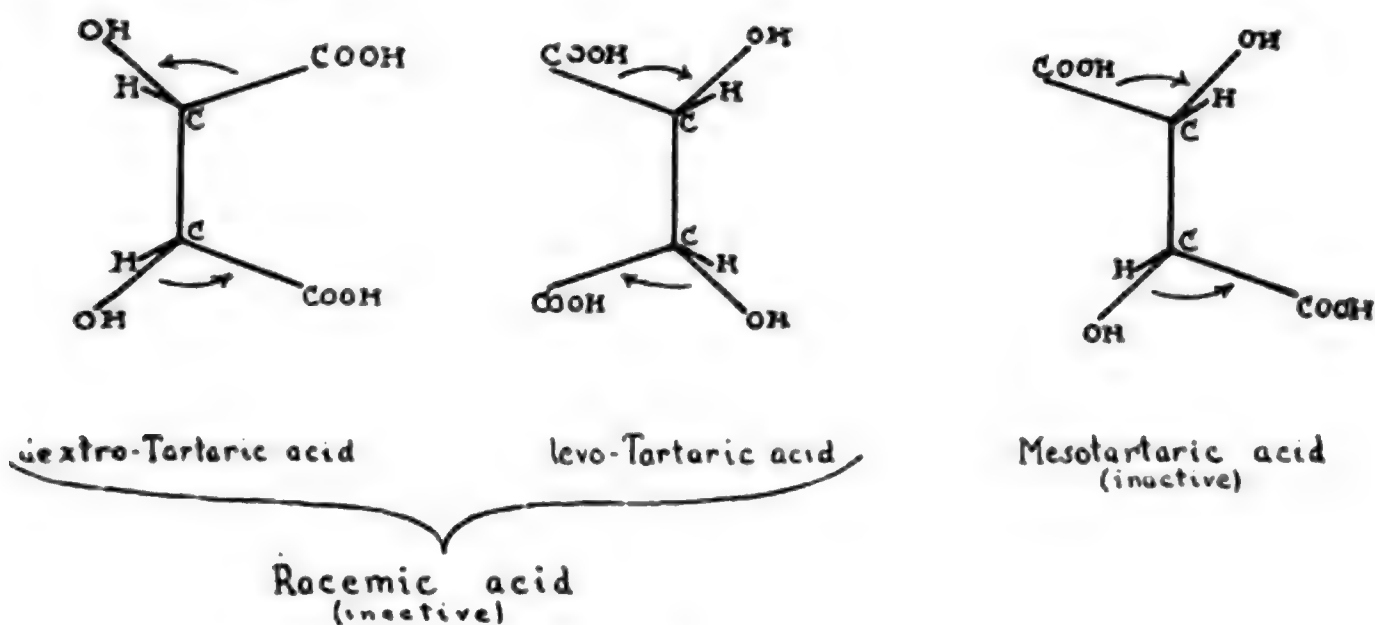


FIG. 6.

The **dextro tartaric acid** has the three groups, (—COOH), (—OH), (—H) linked to each of the asymmetric carbons, arranged in a *right handed* manner in *both of the asymmetric groups*. The **levo tartaric acid** has, similarly, a *left handed* arrangement in *both of the asymmetric groups*. The **racemic acid** consists of *equal molecules of these two active forms* and is thus *optically inactive*, and is able to be split into its optically

active components. The dextro and levo forms are also enantiomorphs, *i.e.*, object and image forms, non-super-imposable. If, however, the three groups, (—COOH), (—OH), (—H), linked to *one asymmetric carbon atom* are arranged in a *right handed* order while those linked to the *other asymmetric carbon atom* are in a *left handed* order, as in the third drawing above, we would expect an *inactive* compound to result in that one-half of the molecule would balance, or neutralize optically, the other half. Such a compound *can not be split into optically active components* without the destruction of the molecule. It is termed *inactive by intra-molecular compensation*. These ideas all agree with the facts as known in respect to the four forms of tartaric acid. This, then, is the extension of the tetra-hedral theory of **van't Hoff** and **Lebel**, as applied to the stereo-isomerism of tartaric acid and as has been found to apply, with equal fitness, to the case of all compounds containing more than one asymmetric carbon atom.

Historical, Pasteur.—The history of stereo-isomerism and the tetra-hedral theory is so intimately connected with tartaric acid that it will be well, at this time, to give a brief outline of it.

In 1820 **Sir John Herschel**, in considering the question of the different optical rotation of crystalline substances, suggested that it might be connected with an unsymmetrical form of crystallization. Later, **Pasteur** in 1848 while studying the salts of tartaric acid recalled this suggestion of **Herschel** and also a statement by **Mitscherlich** to the effect that the crystalline form of ordinary **tartaric acid** which is *dextro* rotatory is identical with that of **racemic acid** which is *inactive*. At that time the two tartaric acids just mentioned were the only ones known.

On studying the sodium-ammonium salt of ordinary tartaric acid (*dextro* tartaric acid), to see if there was any indication of unsymmetrical crystalline form with which to connect the optical activity, according to the suggestion of **Herschel**, **Pasteur** observed that the crystals possessed *hemi-hedral facets*. These gave to the crystals an unsymmetrical form. He then turned his attention to the second known tartaric acid, *viz.*, **racemic acid**, which is optically inactive. His expectation was that in this acid no such unsymmetrical form would exist as it did not possess optical activity. But to his surprise he found, in the crystals of the sodium-ammonium salt, the *same hemi-hedral facets* that he had just found in the salts of the active acid. On closer examination,

however, he observed—and *this is the striking and important thing in his whole investigation*—that the crystals were not all alike. While some possessed hemi-hedral facets on *one side* others had these facets on the *other side, i.e.*, the two forms of crystals were, as is termed in crystallography, *enantiomorphs*, or, *object and image forms*, like the *right hand* and the *left*. On carefully separating these two forms of crystals he found that those of one form, when dissolved in water, gave a solution which rotated the plane of polarized light to the *right*. In other words, one form of crystals was identical with the salt of *dextro* tartaric acid. The crystals which showed the hemi-hedral facets on the other side, when put into solution gave an optical rotation in the *opposite* direction, *i.e.*, to the *left*. Furthermore, on *mixing the solutions of the two forms* of crystals, he obtained a solution that was *inactive*, like the solution of the original **racemic acid** salt with which he started.¹

Thus from a study of the crystalline sodium-ammonium salt of racemic acid and of dextro tartaric acid **Pasteur** showed, conclusively, the relationship of these two acids to each other and also discovered the existence of a third isomer optically active but of opposite direction to the ordinary tartaric acid already known. Racemic acid, therefore, is optically inactive because it consists of equal molecules of the ordinary dextro tartaric acid and the newly discovered levo tartaric acid. Also racemic acid can be resolved into its optically isomeric components by mechanically separating the two forms of crystals of the sodium-ammonium salt. The two active forms of tartaric acid, when mixed in equal molecular amounts, yield the inactive or racemic acid. Later, **Pasteur** prepared the fourth variety of tartaric acid, viz., **meso-tartaric** acid, by heating the cinchonine salt of dextro tartaric acid. This new acid proved to be *inactive* like racemic acid, but, unlike it, was *unable to be resolved into optically active components*. Its relation to the other three forms of tartaric acid was unexplained by **Pasteur**.

In 1873 **Wislicenus** made the suggestion that in compounds like lactic acid and the tartaric acids in which isomers have the same structure but differ in physical properties, *e.g.*, in their rotation of polarized light, the only explanation is that the atoms of the molecules are *differently arranged in space*. Now, in considering this suggestion in con-

¹ See **Pasteur**, "Molecular Asymmetry," Alembic Club Reprints, and Ann. Ch., (3) 28, 56, 1850; Ann., 88, 212, 1853; also, "Life of Louis Pasteur," by Valery Radot.

nection with the relation of known optically active compounds, **van't Hoff** advanced his *theory of the asymmetric carbon atom* and the *tetra-hedral formula* as an explanation of the space configuration of compounds of this nature, *i.e.*, optically active like lactic acid, tartaric acid, etc. At the same time, **LeBel**, in considering the work of **Pasteur**, arrived at practically the same idea though **van't Hoff** assigned a definite tetra-hedral structure to the carbon atom in space, while **LeBel** simply assumed an unsymmetrical grouping of a carbon atom when linked to four different groups or elements. The theory is thus known as the **van't Hoff-LeBel theory of the asymmetric carbon atom and the tetra-hedral configuration**. According to this theory the existence of the fourth variety of tartaric acid, *viz.*, mesotartaric acid, is fully explained as inactive by intra-molecular compensation. The connection of tartaric acid with the development of our ideas of stereo-chemistry is retained in the application of the term, *racemic*, to all compounds which, like racemic acid, are optically inactive, and resolvable into two opposite optically active isomers. Such an inactive form of any compound is termed its *racemic variety*.

Splitting Racemic Compounds.—The methods by which racemic compounds may be split into their optically active components are several. The three methods used were all originated by **Pasteur**. The *first method* has been referred to and consists of the *mechanical separation* of the two oppositely hemi-hedral forms in which the salts of a racemic compound crystallize. This method is especially applicable in the case of tartaric acid when the sodium-ammonium salt is used. The crystallization and separation must be carried out under definite conditions. If the racemic acid salt is crystallized below 28° the two forms of crystals are produced and a separation can be accomplished. If, however, the crystallization takes place above 28° the two forms of crystals are not produced but the sodium-ammonium racemate crystallizes in unseparable crystals of one form. That is, above 28° the sodium-ammonium racemate crystallizes as such, while, below 28° the racemate splits into its two isomeric components and equal amounts of the sodium-ammonium dextro tartrate and the sodium-ammonium levo tartrate are formed. The *second method* for the splitting of a racemic compound into its optically active components consists of the formation of the **cinchonine**, **strychnine**, or other similar alkaloid salts. When the cinchonine salt of racemic acid is formed it splits into the

cinchonine salts of dextro and levo tartaric acid. These two salts do not crystallize in different forms which permit their mechanical separation, but they crystallize at different concentrations. The salt of the levo tartaric acid crystallizes out first and may be separated. Afterward the salt of the dextro tartaric acid crystallizes and may then be obtained by itself. Thus by a *fractional crystallization of the alkaloid salts* of racemic compounds they may be separated into their optically active components. The *third method* for the splitting of racemic compounds is known as the *biological method*. It rests upon the relation of the different acids or salts to certain lower organisms, especially the molds. When the mold, *Penicillium glaucum*, is grown in a solution of ammonium racemate, or some other racemic salt, it uses as nutritive material the ammonium dextro tartrate which becomes, therefore, destroyed and removed from the solution. The ammonium salt of the levo tartrate is, however, not used by the organism and remains in the solution. After the action the solution yields, on crystallization, crystals of the levo tartrate only. Thus by the destruction and removal from the solution of the racemate of one of the optically active components, by means of molds, the other isomer is obtained in the pure form.

Dextro Tartaric Acid

Dextro tartaric acid is the ordinary tartaric acid as it is found widely distributed in nature, in grapes, mountain ash berries, pineapples, potatoes and other plants. It crystallizes without water of crystallization in transparent, mono-clinic columns which are easily soluble in water or in alcohol. 100 parts of water at 15° dissolve 132 parts of the acid. It melts at 168°–170°. In water solution it is dextro rotatory. The chief source of tartaric acid is the juice of the grape, where it is present as the *free acid* and as the *acid potassium salt*. In this source it is mostly the dextro variety that is found. It is obtained from the *vinasse*, or residue which settles out from the juice after it has been expressed. When grape juice ferments, in the formation of wine, the solubility of the acid potassium salt is lessened due to the presence of alcohol and it gradually separates and settles to the bottom in the form of what is known as *lees*. These lees are dried or recrystallized once and the product is then known as *crude tartar* or **argol**. The crude tartar contains, in addition to the acid potassium tartrate, free tartaric

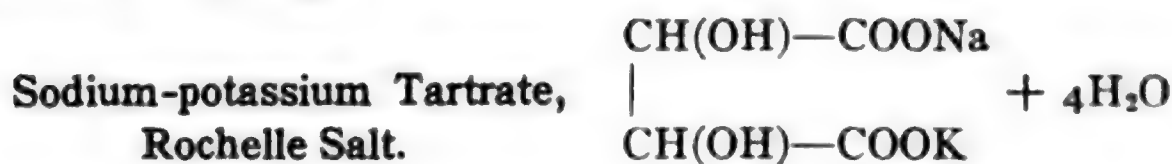
acid and calcium tartrate. By recrystallization and purification the pure acid potassium tartrate is obtained. In the pure form this salt is known as *cream of tartar*. The English name of the acid is derived from its relation to this tartar, *i.e.*, **tartaric acid**. The German name of the acid, *viz.*, **Wein-säure**, is derived from the fact that it separates out when wine is formed. The free dextro tartaric acid is obtained from either the crude or the pure tartar by first treating with milk of lime and subsequently with calcium sulphate. This forms the calcium salt which is then decomposed by means of sulphuric acid and the tartaric acid set free. This is then recrystallized and obtained in the pure form.

The synthetic transformation of dextro tartaric acid into malic, succinic and maleic acids has already been spoken of. When heated to its melting point dextro tartaric acid is converted into meso-tartaric acid. This conversion also takes place when a solution of dextro tartaric acid is evaporated. When it is heated with water to 175° dextro tartaric acid yields both racemic acid and meso-tartaric acid. Long heating with hydrochloric acid yields racemic, meso-tartaric and pyro-tartaric, (methyl succinic) acids. By distillation it yields pyro-tartaric acid and other acids. Tartaric acid reduces ammoniacal silver solution and can be used for silvering purposes. In this reaction the tartaric acid is oxidized to oxalic and other acids. When tartaric acid, or a salt, is heated a characteristic odor of burnt sugar is observed. The free acid is used as a cheaper substitute for citric acid in beverages. It is also used as a mordant in dyeing, and in medicine and photography.

Salts.—Several of the salts of dextro tartaric acid are important.



This salt has already been referred to as **cream of tartar**. It forms rhombic crystals which are only slightly soluble in water. One of its important uses is as a constituent of baking powders. In such powders the other constituent is **sodium acid carbonate**. It is also used as a mordant in dyeing.



This salt crystallizes in thick columns with four molecules of water. Its chief use is as a reducing agent. It reduces an ammoniacal silver solution and in this way is used in silvering glass. It is also used as a constituent of **Fehling's solution**, (p. 332), which is an alkaline copper solution reduced by certain sugars. It acts as a purgative in **Seidlitz powders** which consist of sodium-potassium tartrate, sodium acid carbonate and free tartaric acid.



This salt is used in medicine as an emetic. It is also used in dyeing.

Levo Tartaric Acid

Levo tartaric acid, the optical isomer of dextro tartaric acid, was discovered, as already stated, by **Pasteur** in 1848. It has the same solubility and melting point as the dextro acid. It crystallizes without water of crystallization in the form enantiomorphic to the dextro acid. Its optical rotation is the same in amount but opposite in direction to the dextro acid. When mixed in equal molecular amount with dextro tartaric acid it yields racemic acid. Its synthetic reactions have been considered. It has no common uses.

Racemic Acid

Racemic acid, the resolvable inactive tartaric acid, was discovered in 1820 and was shown to be tartaric acid in 1830. It crystallizes in tri-clinic needles containing one molecule of water, per unit molecule of $C_4H_6O_4$. In this it differs from the dextro and levo forms. The water free acid melts at 205° – 206° , the hydrous crystals melting at 203° – 204° . At 15° 100 parts of water dissolve 17 parts of the acid, it being less soluble than the active forms. While, in concentrated solution the acid exists as a double molecule, the crystals which separate being those of racemic acid, in dilute solution the acid exists as equal molecular parts of dextro and levo tartaric acid. These facts are shown by the results of freezing point determinations. Racemic acid is found, together with dextro tartaric acid, in grapes. Its English name is derived from *raceme*, indicating a bunch of grapes. The

German name, **Trauben-säure**, is derived from the word for grapes. It is probable that it does not exist in grapes as racemic acid but that it is formed from the dextro acid as this transformation can easily be effected by the action of acids or even by water alone. When tartaric acid is prepared synthetically from succinic acid, from glyoxal, or from malic, maleic or fumaric acids either racemic acid or meso-tartaric acid is always formed. That is, synthetic reactions result in the formation of an inactive form. The methods of splitting racemic acid into its optically active components has been fully discussed. The sodium-ammonium racemate is the only salt that is of importance. This has been spoken of in connection with the method of splitting racemic acid into its components. Like the free acid this salt exists, in dilute solution, as equal molecular parts of the dextro and levo forms. Only in concentrated solution does it exist as the racemate itself.

Meso-tartaric Acid

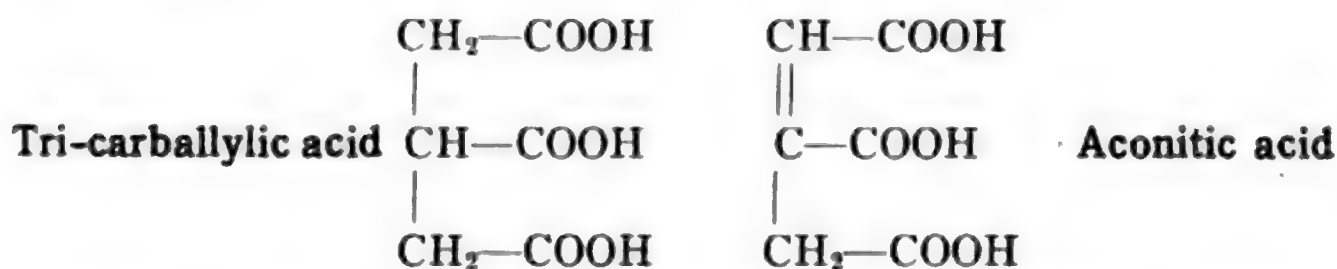
This acid, the inactive by intra-molecular compensation and unresolvable into optically active components, was first obtained by **Pasteur** by heating the cinchonine salt of dextro tartaric acid, to 170° . It may also be prepared by boiling the dextro tartaric acid with an excess of hydrochloric acid, or with sodium hydroxide. Also by long boiling with water alone or by heating with a small amount of water to 165° . When di-brom succinic acid is treated with silver hydroxide, or when malic acid is oxidized, in the presence of water, both meso-tartaric acid and racemic acid are formed. When meso-tartaric acid is heated to 200° it is partly converted into racemic acid. Meso-tartaric acid crystallizes in rectangular plates with one molecule of water. The water free acid melts at 140° – 145° .

IV. TRI-BASIC ACIDS AND HYDROXY TRI-BASIC ACIDS

Tri-carballylic Acid and Aconitic Acid

Tri-basic, *tetra-basic* and *penta-basic* acids are known but most of them are not of sufficient importance to consider at any length. We shall simply mention and give the formulas for two members of the first group. Two tri-basic acids are found in the juice of sugar cane or in the residue which settles out when the sugar cane juice is evaporated. The two acids are both related to **citric acid** which we shall consider next. They are known as **tri-carballylic acid** and as **aconitic acid**.

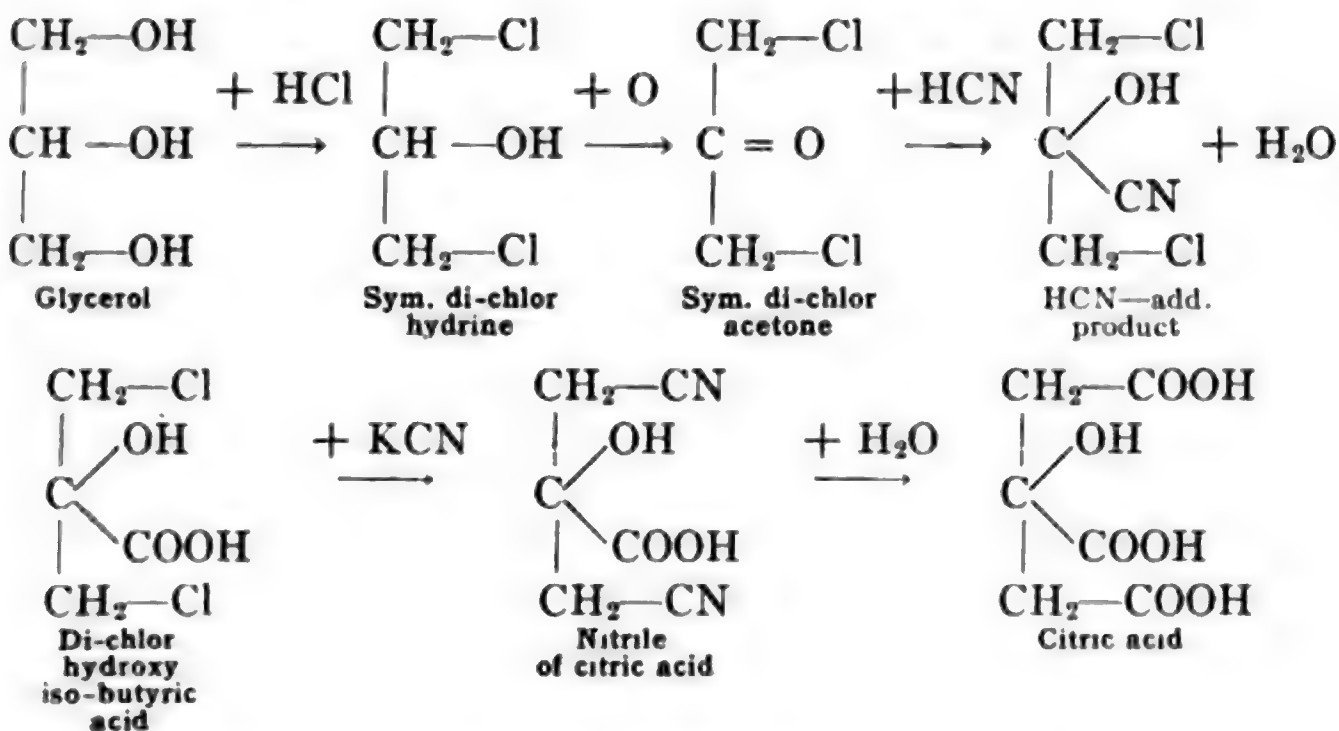
The first has been proven to have the constitution of *1-2-3-tri-carboxy propane* and the second is the unsaturated double bond acid derived from the first. The formulas are as follows:



The two acids may be converted into each other by the appropriate reactions for passing from saturated to unsaturated compounds, or the reverse.

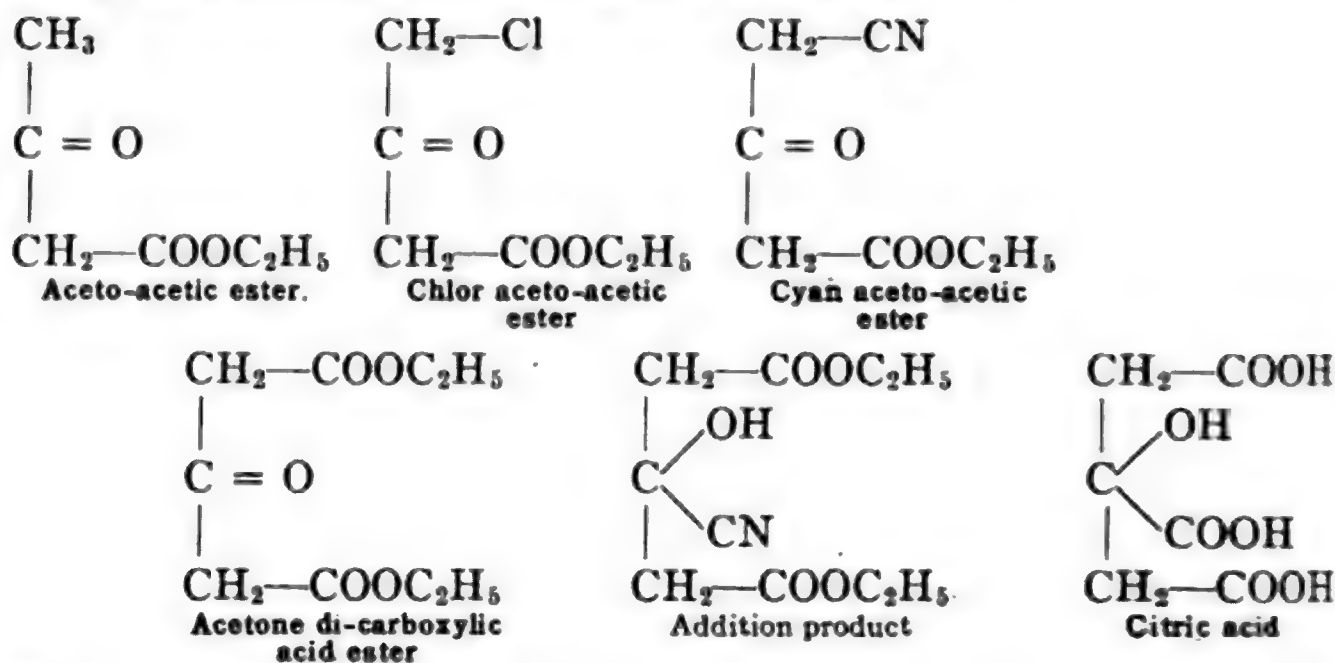
Citric Acid

Synthesis from Glycerol.—Citric acid is related to the two preceding acids and its constitution has been established by two syntheses, one from **glycerol** and the other from **aceto-acetic ester**.



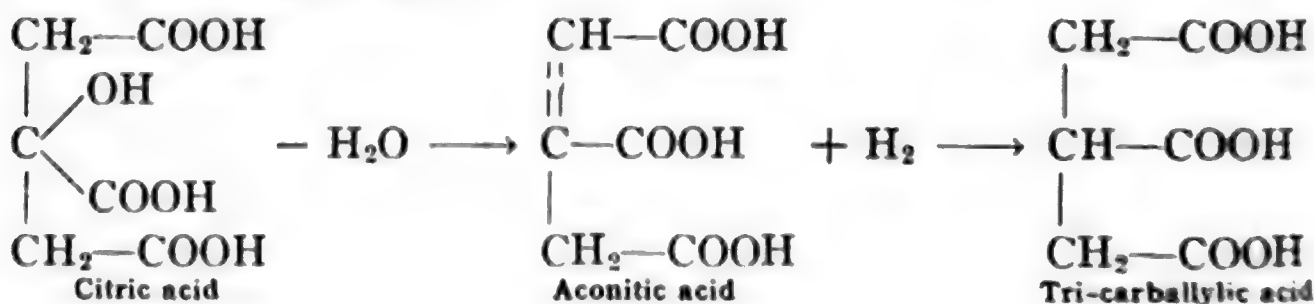
The glycerol is converted into the symmetrical, or, **1-3-di-chlor-hydrine**. By oxidation this yields the symmetrical, or, **1-3-di-chlor acetone**, which by the addition of hydrogen cyanide yields the addition product, that on hydrolysis is converted into a hydroxy acid, viz., **di-chlor hydroxy iso-butyric acid**. By treatment with potassium cyanide this yields the corresponding di-cyanide, or *nitrile* of citric acid which on hydrolysis yields **citric acid**.

From Aceto-Acetic Ester.—The synthesis from aceto-acetic ester takes place according to the following scheme:

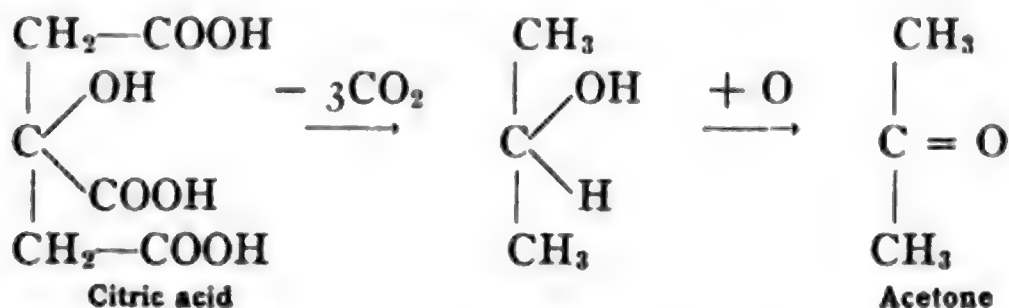


These syntheses establish the constitution of citric as a **2-hydroxy 1-2-3 tri-carboxy propane**, *i.e.*, it is a *tri-basic mono-alcoholic acid*.

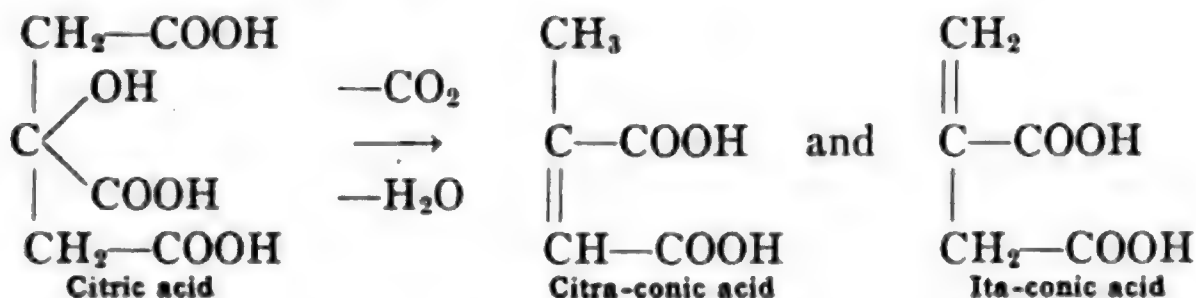
Citric acid is one of the most important plant acids and is widely distributed in various parts of many plants. It is found free, especially in citrus fruits (lemons, limes, etc.), and associated with malic and tartaric acid in currants, goose-berries, raspberries, mountain ash berries, etc. It is also found as the calcium salt in cow's milk and in grape twigs. The chief commercial source is the lemon, where it is present, in the unripe lemon, to about 5 per cent. It is formed when glucose sugar is fermented with a particular mold, *Citromyces citricus*. The chief uses of the acid are as a constituent of lemonade and other beverages, and in the printing of calico prints. It crystallizes in rhombic prisms which contain one molecule of water. The water is lost by heating to 130° and the water free acid melts at 153° . From cold water the acid crystallizes in water free crystals. It is readily soluble in water. When heated to 175° it loses water and is converted into the unsaturated acid, aconitic, which by reduction yields the corresponding saturated acid, *viz.*, tri-carballylic acid.



These reactions show the relation of citric acid to the two tri-basic acids mentioned at the beginning of this section. When subjected to dry distillation citric acid loses carbon dioxide while at the same time it becomes oxidized, and acetone is produced.



In the decomposition by heat other acids are also formed, viz., **ita-conic** and **citra-conic acids** (p. 293). In this case both carbon di-oxide and water are lost,



All of the syntheses and decompositions of citric acid prove its constitution to be as represented.

Salts.—As citric acid is a tri-basic acid it forms three series of salts, e.g., with sodium it yields the *mono*-, *di*- and *tri-sodium* salts, the last being the neutral sodium citrate. Only three salts of citric acid are of importance.

Neutral Ammonium Citrate.—A solution of this salt is used in the analysis of fertilizers to represent the solvent action of plant juices and soil water.

Magnesium Citrate.—This salt is used in medicine as a purgative. Mixed with sodium bi-carbonate, free citric acid and sugar it produces a pleasant effervescing purgative.

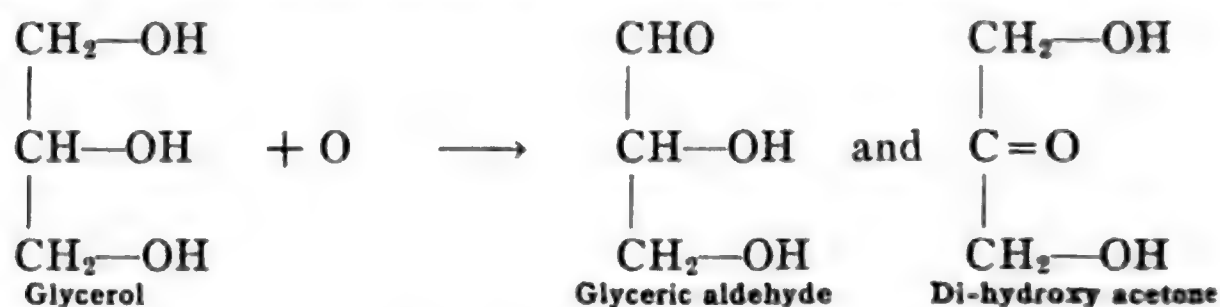
Ferric Ammonium Citrate.—This salt, a soluble salt of iron and ammonia, is used in calico printing and in the blue-print photographic process.

Ferric Citrate.—The single iron salt of citric acid forms colloidal solutions and is used in the study of colloids.

X. CARBOHYDRATES

GENERAL

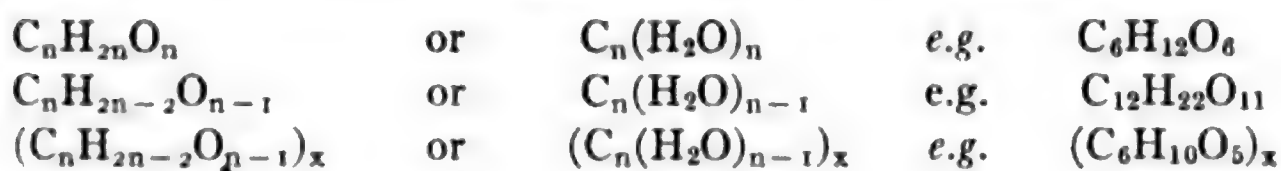
Oxidation Products of Poly-hydroxy Alcohols.—In our study of the mixed poly-substitution products we considered the mixed alcohol-aldehyde and alcohol-ketone compounds and showed that they are intermediate oxidation products between poly-hydroxy alcohols and poly-basic acids (p. 228). To illustrate, when **glycerol, tri-hydroxy propane**, is oxidized the following products are obtained.



The formation of the two products depends upon the fact that in one case, **di-hydroxy acetone**, the *secondary alcohol* group of the glycerol is oxidized to a *ketone* group while in the other case, **glyceric aldehyde**, one of the *primary* alcohol groups is oxidized to an *aldehyde* group. The reason for waiting until this time for the full consideration of these alcohol-aldehyde and alcohol-ketone compounds is, that these compounds and their derivatives constitute that most important group known as the **carbohydrates**, or **sugars**, including such well known substances as **glucose sugar**, **cane sugar**, **starch** and **cellulose**. Because of relationships between them and the di-basic acids and also because of their relation to stereo-isomerisms which we have developed more fully in connection with lactic and tartaric acids, it was best not to take up the carbohydrates until after the poly-basic acids and the hydroxy acids had been studied. We shall first consider the composition and constitution of the carbohydrates wholly independent of the historical development of the facts or of the natural classification of the different members of the group.

Composition and Constitution.—The name *saccharoses* applies in general to all carbohydrates and the termination *ose* is used in the names of most of the different groups and individuals. Whenever

used this termination always means a carbohydrate. The name *saccharide* is often used but the termination *ose* is much to be preferred. The more important carbohydrates have the composition represented by the following general formulas, which apply in all cases except in those of methyl derivatives and the group of *tri-saccharoses*.



That is, carbohydrates, so far as their empirical composition is concerned, are carbon-water compounds. This explains the origin of the name **carbo-hydrates**, *i.e.*, *carbon-water* compounds. This idea that carbohydrates were carbon-water compounds was supported by the fact that on heating or on treatment with a dehydrating agent, like sulphuric acid, the compounds were decomposed into water and carbon. This may easily be shown by simple experiments. On heating sugar in a dry test tube it gradually chars and gives off water until only carbon is left. Also, when dry sugar is treated with sulphuric acid it chars in a like manner and a residue of pure carbon remains. The simplest group, with the general formula $C_nH_{2n}O_n$, embraces sub-groups which contain different amounts of carbon varying from *three* to *nine* atoms to the molecule. They are termed *simple carbohydrates*, *simple sugars* or *mono-saccharoses* and the names of the sub-groups are made from the termination *ose*, together with the numerical prefix indicating the number of carbon atoms present. We have, therefore, as follows:

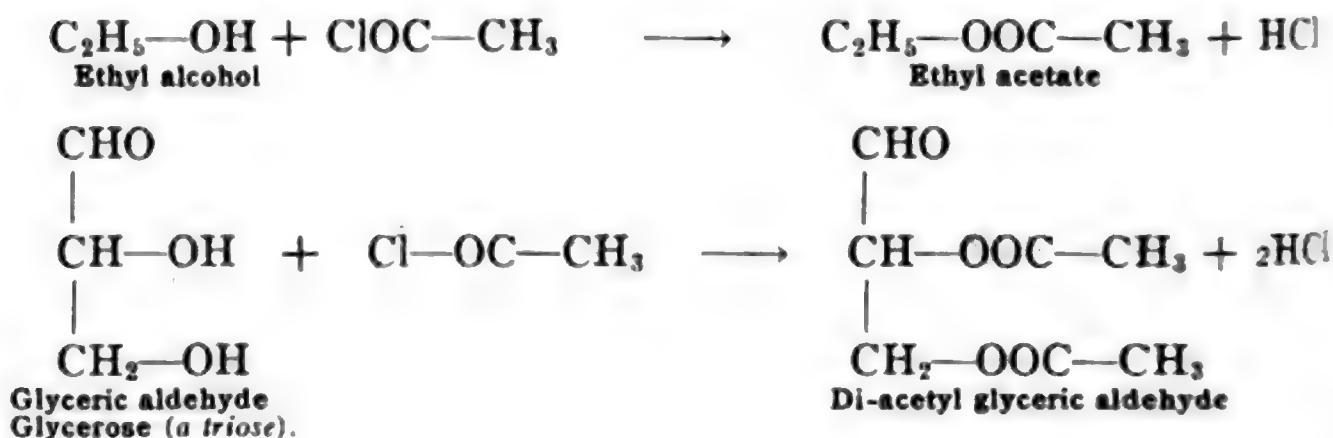
Simple Carbohydrates,	$C_nH_{2n}O_n$
<i>Mono-saccharoses</i>	
<i>Tri-oses,</i>	$C_3H_6O_3$
<i>Tetroses,</i>	$C_4H_8O_4$
<i>Pentoses,</i>	$C_5H_{10}O_5$
<i>Hexoses,</i>	$C_6H_{12}O_6$
<i>Heptoses,</i>	$C_7H_{14}O_7$
<i>Octoses,</i>	$C_8H_{16}O_8$
<i>Nonoses,</i>	$C_9H_{18}O_9$

It is necessary to state this much in regard to the simple sugars, before taking them up in detail, because, in developing our ideas of con-

stitution and in studying the general reactions of the carbohydrates as a whole, we must use some of these compounds as illustrations.

The relation between carbon, hydrogen and oxygen in the composition of the carbohydrates shows nothing, however, as to the constitution of the compounds except that it indicates the probable presence of *secondary alcohol* groups, ($=\text{CH}(\text{OH})$), which, it will be observed, have the same relative amounts of the three elements in question. It is impossible to conceive, however, of a compound as built up of secondary alcohol groups only.

Alcohol Compounds.—That the carbohydrates are, in fact, alcohol compounds is shown, both by their relation to poly-hydroxy alcohols and by their reactions. Carbohydrates possess alcohol characters in that they undergo distinctly alcoholic reactions. Like all alcohols they react with **acetyl chloride** or **acetic anhydride**. In practice the latter reagent is used. They form acetyl derivatives, or esters, just as ethyl alcohol does.



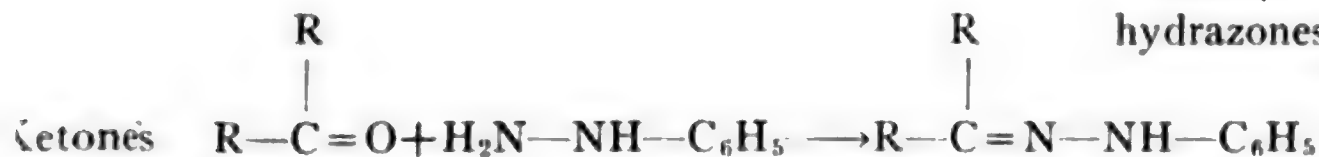
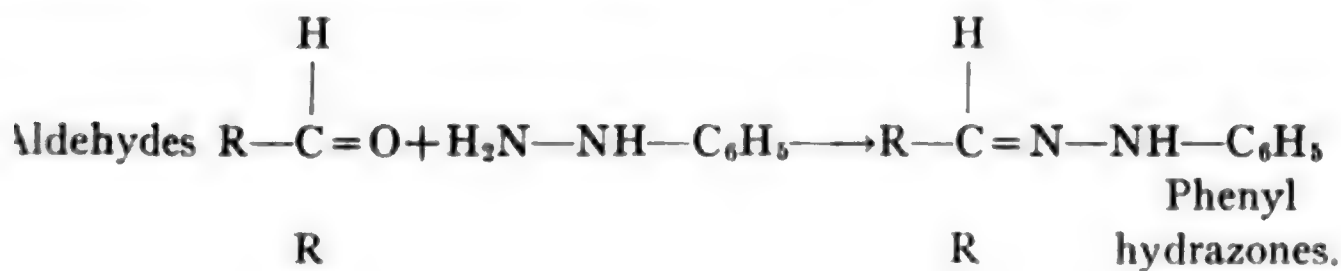
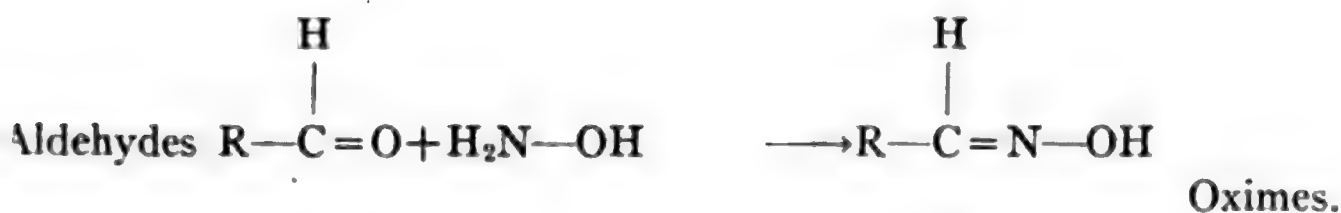
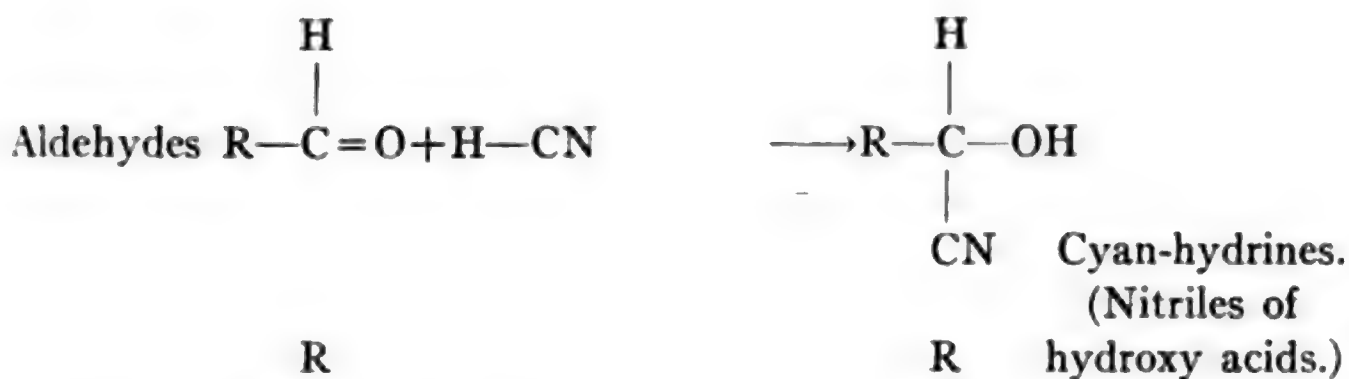
Esterification or Acetylation.—This reaction is of especial importance, because it not only proves the presence of hydroxyl groups but, it determines their number, for complete acetylation introduces as many acetyl groups as there are hydroxyl groups in the original compound.

Number of Hydroxyl Groups.—In this way it has been shown that in the simple carbohydrates the *number of hydroxyl groups is one less than the number of carbon atoms*. As more than one hydroxyl group is not usually linked to one carbon the indication is that *each carbon atom but one has one hydroxyl group linked to it*. That the remaining carbon atom is in a *carbonyl* grouping was first established by **Kiliani**, who showed that in water solution the carbohydrates are *aldehyde or ketone* compounds as well as poly-hydroxy alcohols.

Aldehyde or Ketone Compounds.—This aldehyde or ketone constitution is proven by several reactions.

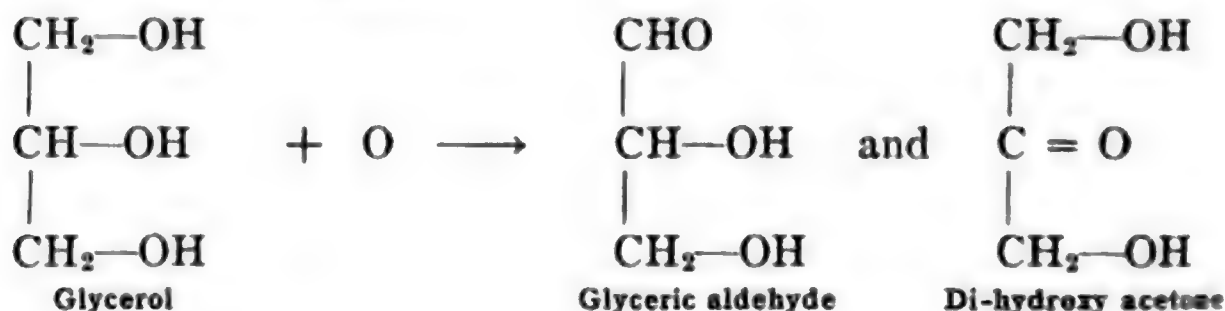
Aldehyde and Ketone Reactions.—(1) The formation of *addition products* with **hydrogen cyanide**, H—CN . (2) The formation of *oxime compounds* with **hydroxyl amine**, $\text{H}_2\text{—NOH}$. (3) The formation of *hydrazone compounds* with a benzene compound known as **phenyl hydrazine**, $\text{H}_2\text{N—NH—C}_6\text{H}_5$.

These three reactions are all characteristic of compounds which contain the carbonyl group, *i.e.*, *aldehydes* or *ketones* (p. 125). They may be illustrated as follows:



All of these reactions as given above for aldehydes and ketones in general, take place with the simple carbohydrates when they are in solution in water and constitute the chief proof that in such solution they are aldehyde or ketone compounds.

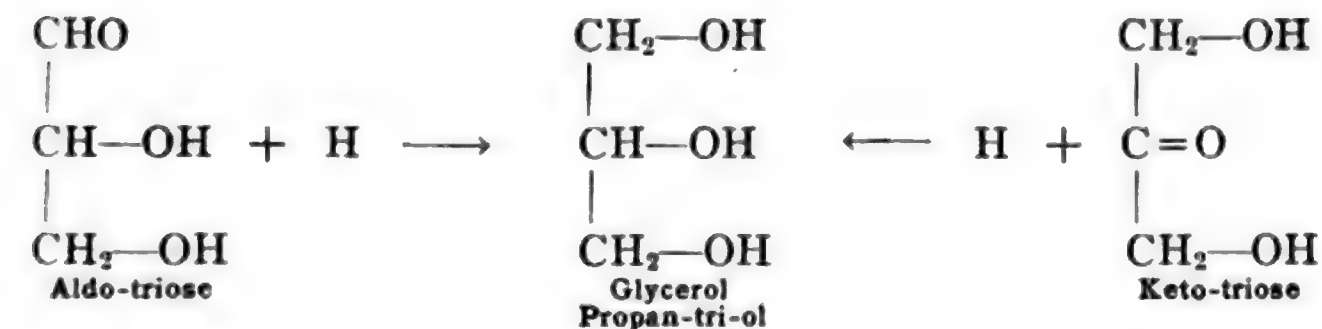
Synthesis.—The carbohydrates have been prepared synthetically by oxidizing the poly-hydroxy alcohols. We have recently spoken of the mixed alcohol and aldehyde or mixed alcohol and ketone compounds which are formed by the oxidation of the tri-hydroxy alcohol glycerol. We have, also, just stated that the carbohydrates have been proven to be mixed poly-hydroxy alcohols and aldehydes or ketones. The compound just referred to, as produced by the oxidation of glycerol, is the simplest compound which has the character of a true sugar. Its composition is in accordance with the first of the general formulas, viz., $C_3H_6O_3$ or $C_nH_{2n}O_n$, and from the number of carbon atoms present it would be termed a **triose**. The oxidation of glycerol results in a mixture of two compounds, viz., an *aldehyde alcohol* and a *ketone alcohol*.



Glycerose.—Glycerose, $C_3H_6O_3$, a *triose*, is a mixture of these two definite compounds, glyceric aldehyde and di-hydroxy acetone. It is the simplest carbohydrate possessing the general character of a sugar. It was discovered by **Deen** in 1863. It reacts with acetic anhydride, forming acetyl derivatives in which the alcoholic hydroxyls are the reacting groups. It also reacts with hydrogen cyanide, forming addition products, cyan-hydrines, with the aldehyde or ketone groups. The aldehyde or ketone groups also react with phenyl hydrazine forming hydrazones and with hydroxyl amine yielding oximes. Glycerose, as it has been obtained, is not a single compound but a mixture of two, one being an aldehyde and the other a ketone. It seems probable that either of these compounds alone is a true carbohydrate but at present we know this simplest sugar only as a mixture of the two. In the case of the higher members of the simple carbohydrates containing four to nine

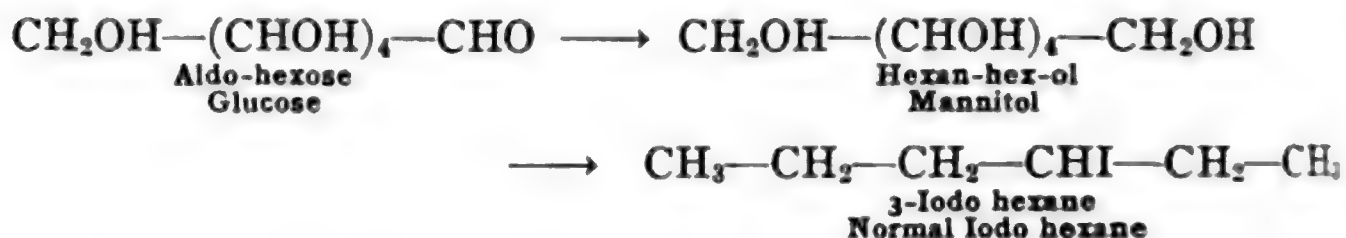
carbons, we find in each two distinct compounds, just as in glycerose, but in all cases except glycerose, each compound, by itself, is a true *carbohydrate* and is also a true *sugar* in its general properties such as taste. Thus we have two different kinds of simple sugars, viz., *aldehyde sugars* and *ketone sugars*. To distinguish between these and to retain the termination *ose* for all carbohydrates, the terms *aldose* and *ketose* are used. Thus while the triose sugar is known only as a mixed aldose and ketose each of the other simple sugar groups, viz., *tetroses*, *pentoses*, *hexoses*, *heptoses*, *octoses* and *nonoses* are known both as an *aldose* and *ketose*. The six carbon sugars, *hexoses*, which are our most common and important sugars, are thus known as two distinctly different compounds. One is an aldehyde sugar or aldose, while the other is a ketone sugar or ketose. We therefore also term the first an *aldo-hexose* and the second a *keto-hexose*. The two compounds are *structural isomers* both having the composition formula $C_6H_{12}O_6$. We shall consider them in detail later on. The first, the *aldo-hexose*, is known as **glucose** and the *keto-hexose* as **fructose**. The reverse of the preceding reaction also establishes the constitution of the carbohydrates.

Reduction.—By reduction they are converted into the poly-hydroxy alcohols containing the same number of carbon atoms.



Straight Chain Compounds.—The poly-hydroxy alcohols, thus obtained from the carbohydrates, may be further reduced, by means of hydrogen iodide, first to the iodine substitution product of the corresponding hydrocarbon and then to the hydrocarbon itself. Thus, we may pass from the carbohydrate to the hydrocarbon corresponding to it and containing the same number of carbon atoms. From glycerose, through glycerol, according to the above reactions, we may obtain propyl iodide and then propane. The important fact is that we obtain, in every case, the *normal hydrocarbon*. This means that the structure of the carbohydrates is that of a *normal chain* of carbon groups.

This may be best illustrated by taking glucose the aldo-hexose, the exact constitution of which we shall develop later,

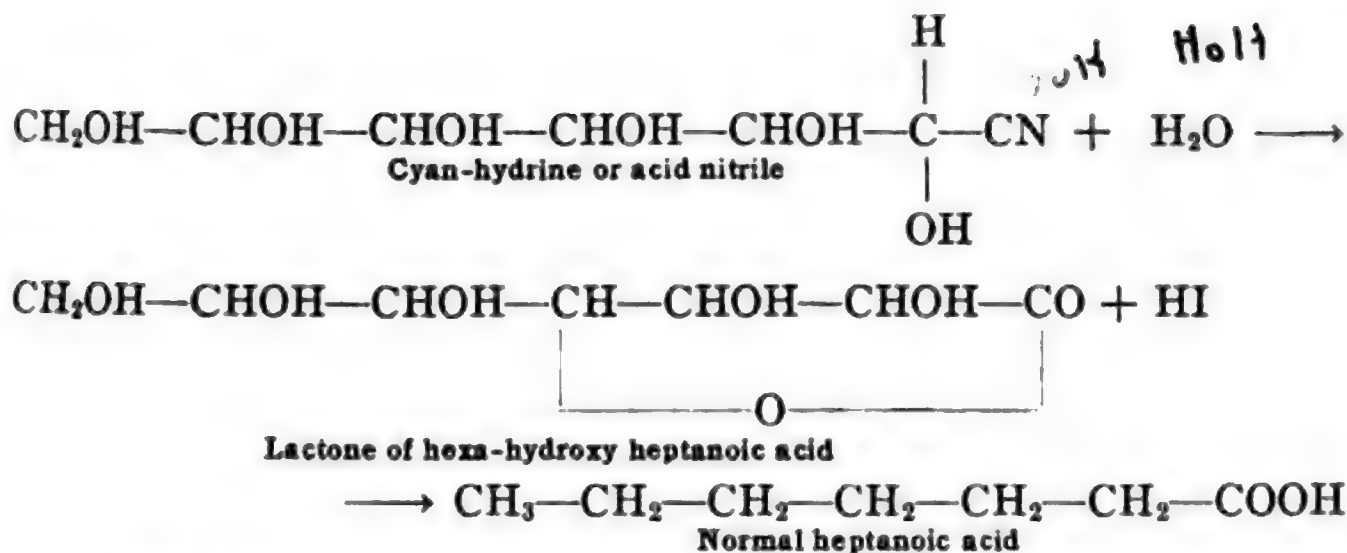


Position of Aldehyde Group.—If, then, the carbohydrates are compounds made up of a *normal chain of carbon groups, each carbon group but one containing one and only one hydroxyl*, and the *remaining carbon group* is a *carbonyl group* (aldehyde or ketone), it remains simply to determine the *position of this carbonyl group*. The character of the hydroxyl grouping, *i.e.*, whether as *primary alcohol* or as *secondary alcohol*, is determined simply by the fact that the *end carbons*, in normal carbon chains, if containing a hydroxyl group, *must always be a primary alcohol group*, and the *intermediate carbons*, in the same kind of chain, *must be secondary alcohol groups*. Therefore, the end carbon groups are the only ones possible of existence as an aldehyde group and the *aldehyde group*, in aldoses, *must be the end carbon group*. Taking therefore, the aldo-hexose glucose as an example, we should write the formula as follows:



We have, however, another proof that the aldehyde group is the end group of the carbon chain. By the addition of hydrogen cyanide a reaction characteristic of the carbonyl group, as previously discussed, we obtain from the aldo-hexose a cyan-hydrine and this cyan-hydrine like all cyanogen compounds, is an *acid nitrile*, which yields, on hydrolysis, an acid which contains, not *six* carbons as the aldo-hexose did, but *seven* carbons. That is, we have increased the number of carbons by one. Furthermore, the acid so obtained is the *normal acid*, viz., **normal heptanoic acid**, $\text{CH}_3-(\text{CH}_2)_5-\text{COOH}$. We do not get the *normal* heptanoic acid, at once, as the result of the hydrolysis but the *lactone of hexa-hydroxy heptanoic acid*, $\text{CH}_2\text{OH}-(\text{CHOH})_5-\text{COOH}$, which by reduction gives us the non-hydroxy normal acid.





In this normal acid the carboxyl group must be joined to the *sixth* carbon and this sixth carbon must be the one which, in the aldose, was in the condition of carbonyl. Thus the aldehyde group in the original aldose sugars must have been the *end group*. The constitution of the aldose sugars is, therefore, as has been written.

Position of Ketone Group.—By exactly the same set of reactions it has been shown, from the structure of the resulting acid, that in the ketose sugars the ketone group is the carbon group *next to the end*. The acid obtained on hydrolyzing the hydrogen cyanide addition product obtained from **fructose** is known as **fructose carboxylic acid** and this on reduction of the hydroxyl groups yields **methyl butyl acetic acid**, $\text{CH}_3-\text{CH}_2-\text{CH}_2-\text{CH}_2-\underset{\text{COOH}}{\text{CH}}-\text{CH}_3$, or **hexane-2-carboxylic acid**.

Also by an oxidation resulting in splitting the chain at the ketone group fructose yields **hydroxy acetic acid**, $\text{CH}_2\text{OH}-\text{COOH}$ and **tri-hydroxy butyric acid**, $\text{HOOC}-\text{CH}(\text{OH})-\text{CH}(\text{OH})-\text{CH}_2\text{OH}$.

We have used hexose sugars for the purposes of illustration but the reactions which we have used, and the type of formulas as proven, apply to all simple carbohydrates whatever the number of carbon atoms.

Constitution.—Let us summarize the proofs for the constitution of the carbohydrates.

1. By the formation of acetyl derivatives and by the reduction to normal hydrocarbons containing the same number of carbon atoms, passing through the poly-hydroxy alcohols of the same number of carbons, carbohydrates are *poly-hydroxy alcohols in which each carbon atom has one and only one hydroxyl group linked to it*.

2. By the reaction with hydrogen cyanide, HCN, forming cyan-hydrines, which are acid nitriles, with hydroxyl amine, H_2NOH , forming oximes, and with phenyl hydrazine, $\text{H}_2\text{N}-\text{NH}-\text{C}_6\text{H}_5$, forming hydrazones, all of which reactions are characteristic of the carbonyl group, carbohydrates in *water solution* are *aldehyde or ketone compounds*.

3. By reduction, with nascent hydrogen (sodium amalgam), forming *normal* poly-hydroxy alcohols, and by the further reduction, by means of hydrogen iodide, HI, forming *normal* iodo-hydro-carbons, carbohydrates are compounds containing a *normal or straight chain of carbon groups*.

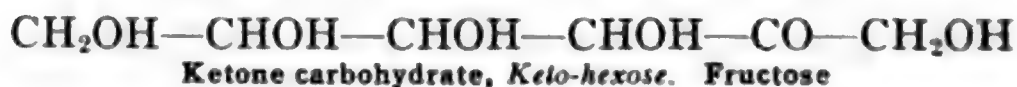
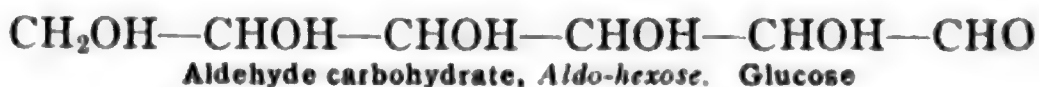
4. By the three preceding reactions and by the formation of carbohydrates by the oxidation of poly-hydroxy alcohols, carbohydrates are *poly-hydroxy alcohols in which one alcohol group is oxidized to aldehyde (primary alcohol group at the end of the chain), or to ketone (secondary alcohol group)*.

5. By conversion, through the cyan-hydrine addition products and the hydrolysis of these into definite acids containing one more carbon than the carbohydrate, carbohydrates are compounds in which the *aldehyde group is at the end of the carbon chain and the ketone group is the second carbon group or the one next to the end*.

That is, *in water solution*:

Carbohydrates are *aldehyde or ketone oxidation products of normal poly-hydroxy alcohols of the same number of carbon atoms, in which one carbon group only is oxidized to aldehyde or ketone, the aldehyde group being the end carbon group and the ketone group being next to the end*.

We may then write the constitutional formulas for the aldo-hexose and the keto-hexose as follows:



This constitution has been shown to hold for all simple carbohydrates and, until recently, has been the accepted constitution. In referring to the aldehyde and ketone structure and the proofs for it we have repeatedly stated that *in water solution* the facts hold as true. Recent study of ether derivatives, known as *methyl glucosides*, formed by reaction with methyl alcohol have shown, however, that for the

actual substances another constitution is undoubtedly the correct one. This new constitution for the carbohydrates will be considered later (p. 345) in connection with glucose and the other hexose carbohydrates. The development of our ideas in regard to the relationship and classification of carbohydrates is, however, better accomplished by accepting this earlier constitution and, as the reactions involved take place in water solution, the aldehyde and ketone constitution holds as true and will therefore be used in the following discussion.

Derivatives of Carbohydrates and Conversion of Carbohydrates

Oxidation to Acids.—By treatment with oxidizing agents the aldose carbohydrates yield products resulting from the oxidation of the end carbon groups. It is interesting that ordinary oxidation affects only these end groups. As one of these may be oxidized at a time we obtain, first, mono-basic acids and then di-basic acids, containing also unoxidized alcohol groups, *i.e.*, *hydroxy mono-basic acids* and *hydroxy di-basic acids*.

When glucose is acted upon by chlorine water, bromine water, silver oxide, or dilute nitric acid, the aldehyde group is oxidized to carboxyl and a mono-basic acid results.



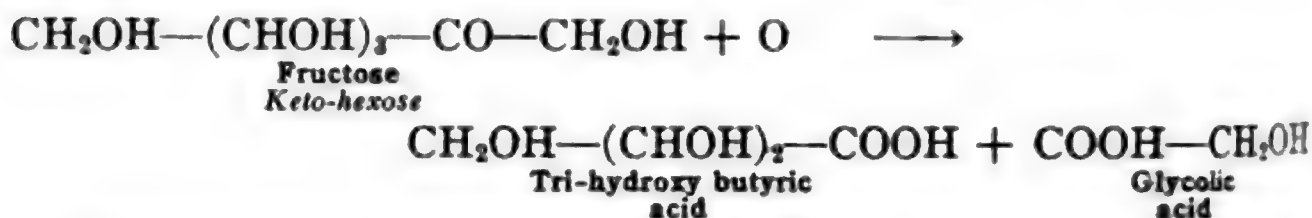
By other reactions another mono-basic acid may be obtained in which the carboxyl group is at the other end of the chain. This is an *aldehyde hydroxy acid* known from its relation to glucose as **glucuronic acid** (p. 253). It is $\text{HOOC}-(\text{CHOH})_4-\text{CHO}$. With strong oxidizing agents, *e.g.*, concentrated nitric acid, the result is a di-basic acid,



Thus, on oxidation, the aldehyde sugars yield hydroxy mono-basic acids and hydroxy di-basic acids of the *same number of carbon atoms*.

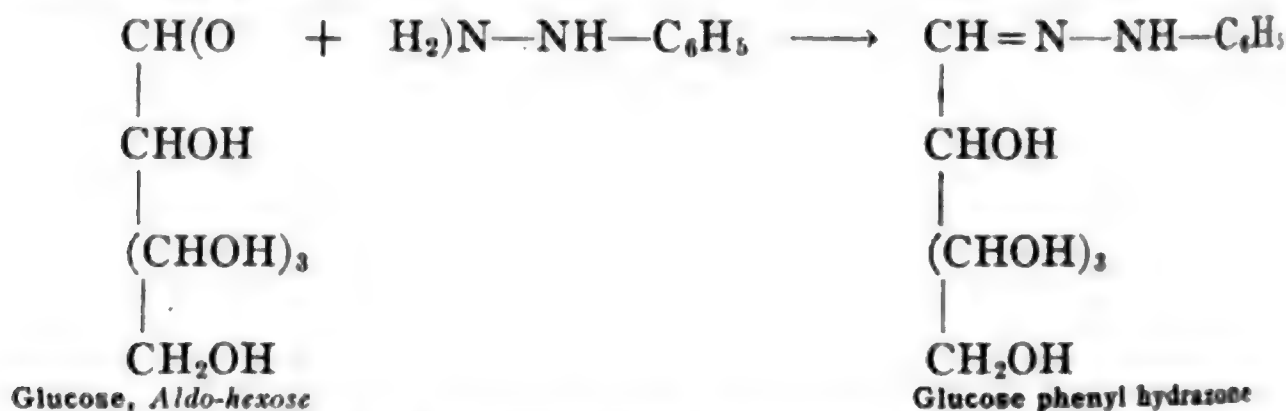
When, however, a ketone sugar is similarly oxidized, the original carbon chain is broken at the ketone group and the acids resulting have a *smaller number of carbon atoms than the carbohydrate*.

The keto-hexose, corresponding to the aldo-hexose given above, is oxidized as follows:

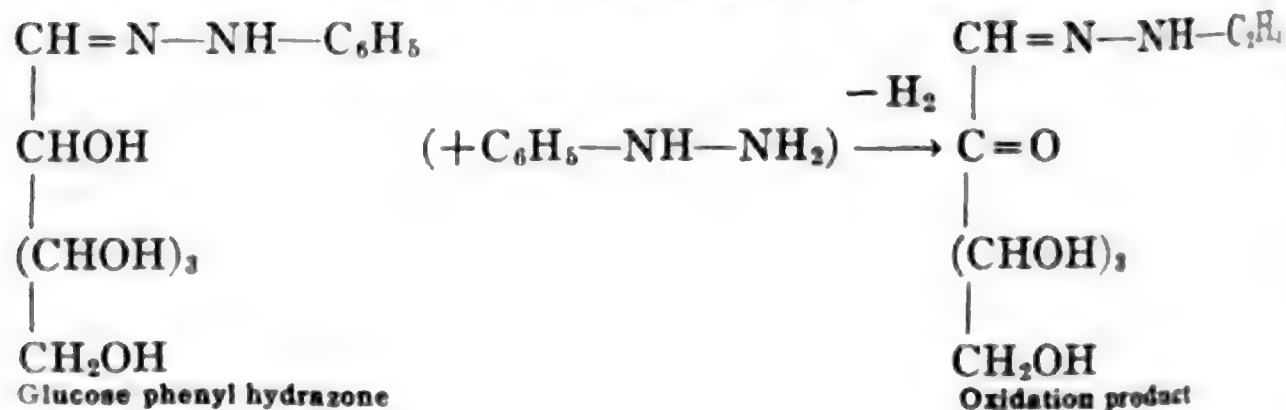


This reaction supports the statement made a short time ago, based on other reactions, that the position of the ketone group is next to the end of the carbon chain.

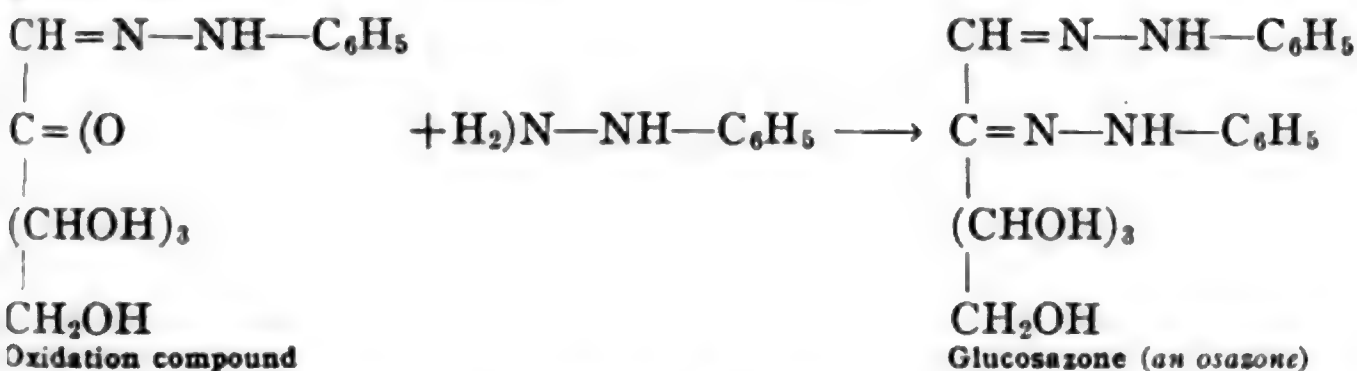
Phenyl-hydrazine Reaction.—Hydrazones.—The reaction with **phenyl hydrazine** has been given as one of the aldehyde or ketone reactions which prove the presence, in sugars, of the carbonyl group. The compounds resulting from this reaction are known as *hydrazones*, or more specifically as **phenyl hydrazones**. With an aldo-hexose the reaction is as follows:



When, however, an aldose sugar is treated with an *excess* of phenyl hydrazine in acetic acid, the reaction does not stop here. A *second molecule* of phenyl hydrazine reacts as an *oxidizing agent*, being reduced itself to other compounds. As a result of this oxidizing reaction one of the secondary alcohol groups of the sugar molecule residue of the hydrazone becomes oxidized to carbonyl. The group oxidized is the one next to the original aldehyde group in the aldose.

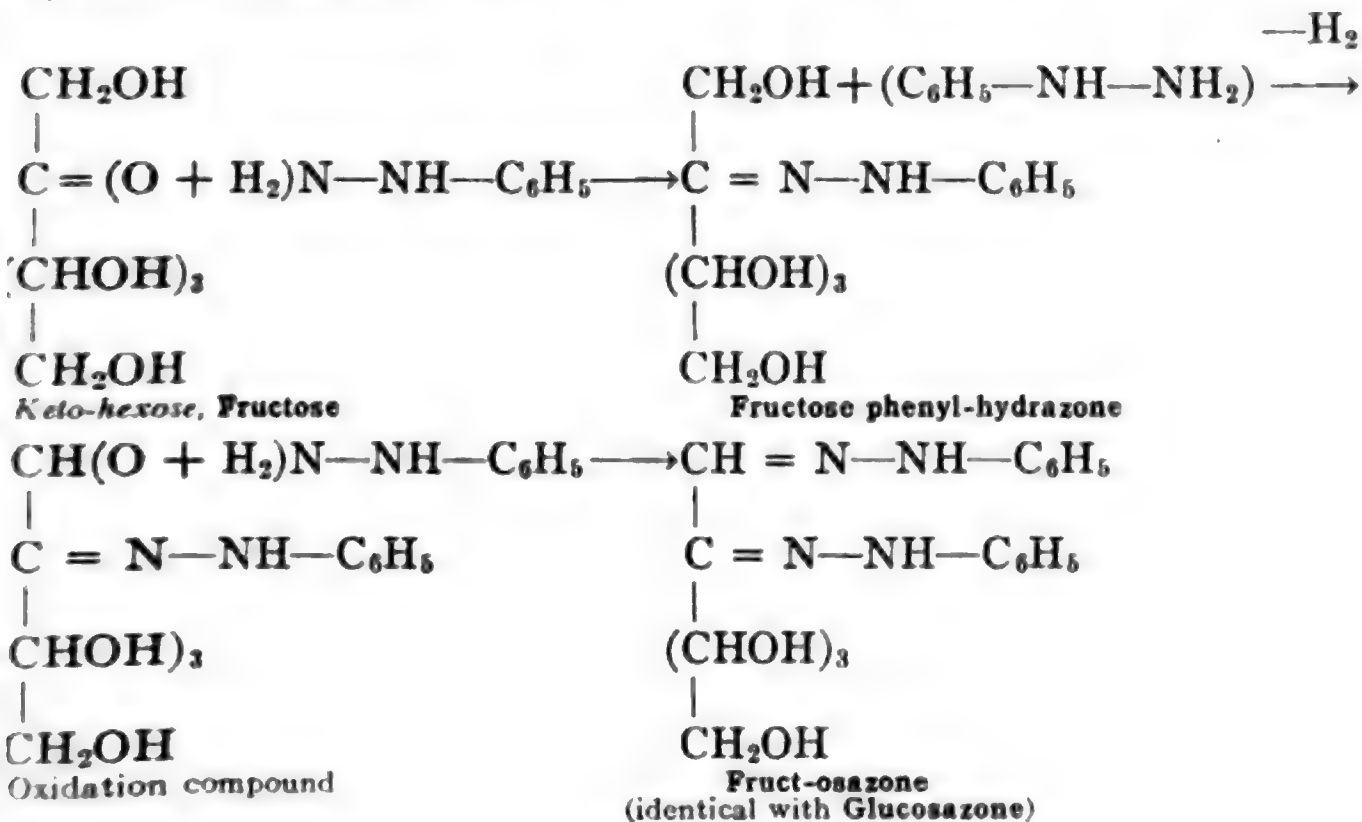


Osazones. Glucosazone.—This intermediate product, the oxidation compound, containing, now, a new carbonyl group, reacts with a *third molecule* of phenyl hydrazine forming a *double phenyl hydrazone* which is known as an *osazone*. From glucose the osazone is known as *glucosazone*.

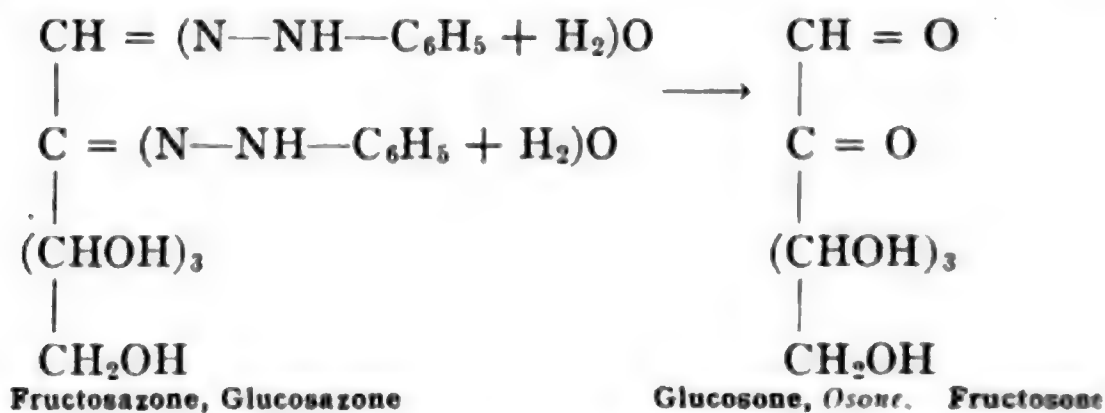


These osazones differ from the first formed hydrazones in being less soluble and more easily crystallized. This makes it possible to separate sugars from each other by converting them into their osazones.

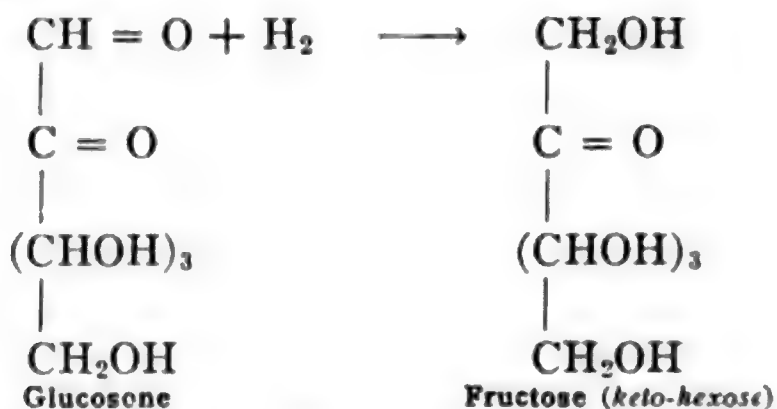
Fructosazone.—The still more important fact is, that the corresponding ketose sugar which has a different structure reacts in a similar way and yields exactly the *same osazone*. This means that in the **tetose phenyl hydrazone** the oxidation by means of the second molecule of phenyl hydrazine converts the end carbon group, next to the ketone group in the original ketose into a new aldehyde group, giving a new carbonyl group at the end of the chain to react with the third molecule of phenyl hydrazine.



Osones.—We are not yet done with the interesting reactions of these compounds for the osazones when warmed with concentrated hydrochloric acid, take up water and split off the two phenyl hydrazine residues and yield a compound containing *both the aldehyde and the ketone groups* of the original aldose and ketose sugars. The resulting compound is known as an *osone*:

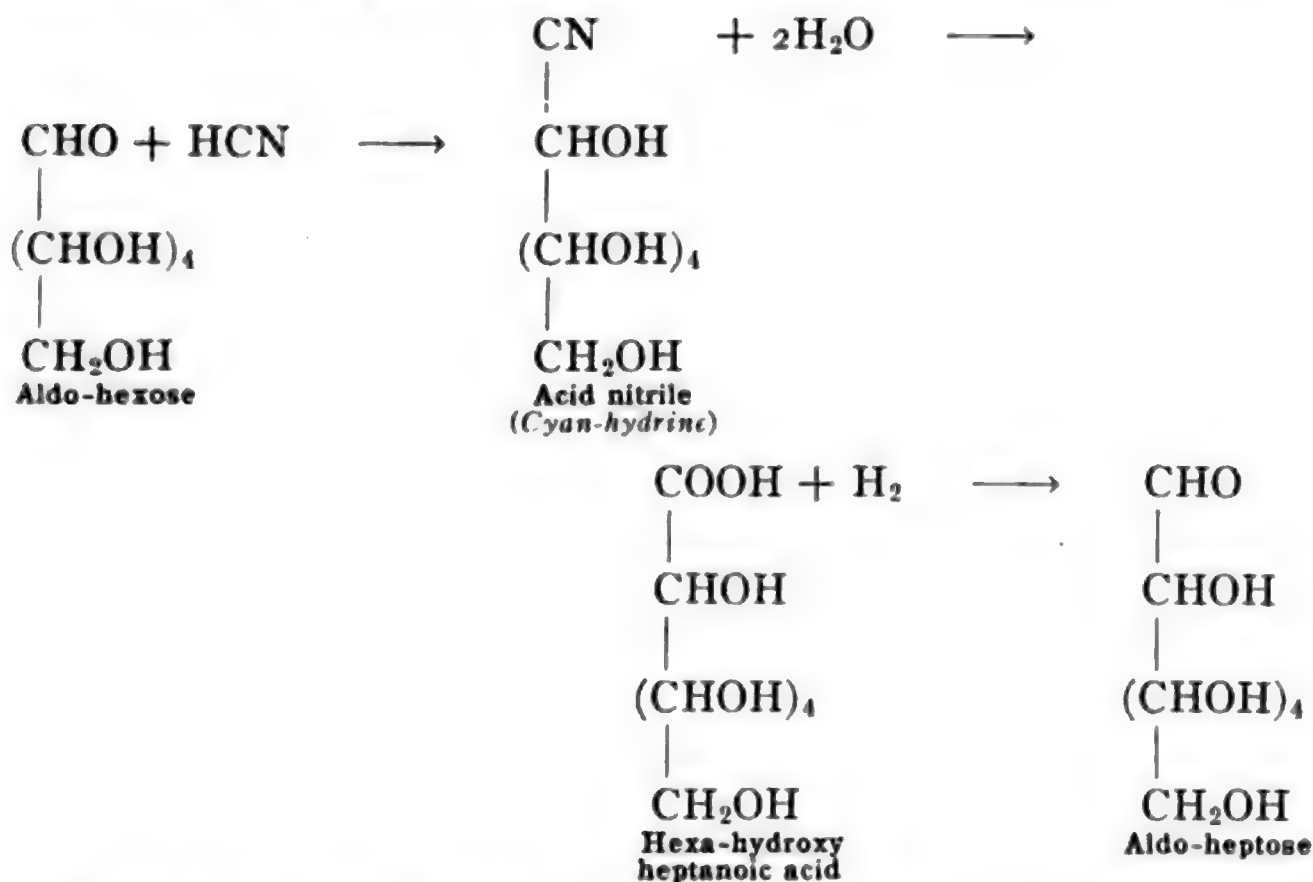


Finally, the osones, by reduction with nascent hydrogen, ($\text{Zn} + \text{CH}_3\text{—COOH}$), have one of the carbonyl groups converted back into the alcohol group and the product is a hexose sugar such as we started with. The important fact, here, is, that it is *always the end carbonyl which is thus reduced so that the resulting sugar is always the ketose sugar*. The reactions are,



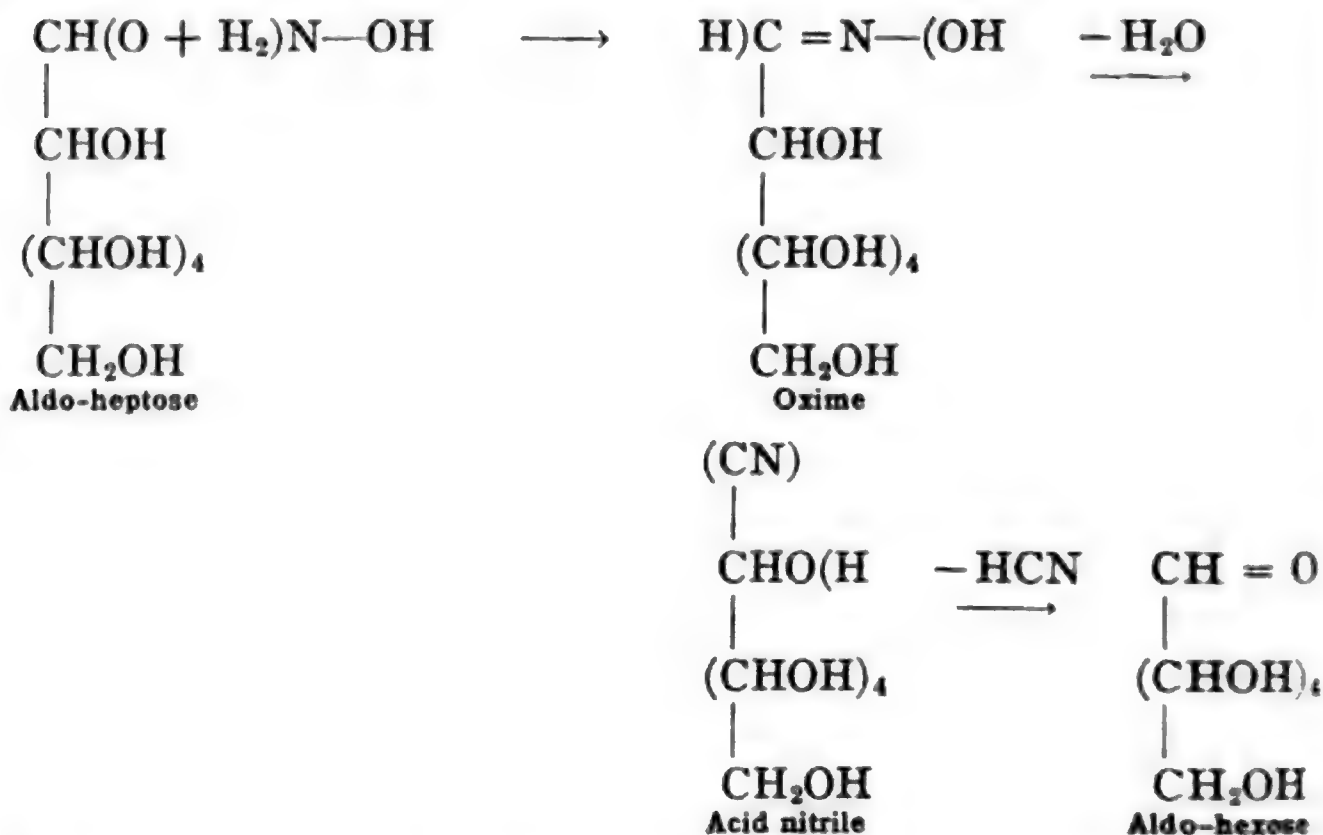
Conversion of Aldose into Ketose.—Therefore, while an aldose sugar and a ketose sugar yield the *same osazone* and the *same osone*, on the reduction of the osone the *ketose sugar is always obtained*. This gives a general method for the *conversion of an aldehyde sugar into the corresponding ketone sugar*. The phenyl hydrazine reaction is thus seen to be a very important reaction in connection with carbohydrates as it enables us to form well crystallized and separable osazones and also to convert any compound belonging to one of the general classes of carbohydrates, viz., aldoses into the isomeric compound of the other general class, viz., ketoses.

Increasing Carbon Content of Aldoses.—The other two aldehyde reactions of sugars, viz., the reaction with **hydrogen cyanide** and the one with **hydroxyl amine** are equally important with the phenyl hydrazine reaction as, by them, we are enabled to convert any aldose sugar into another aldose sugar containing, in the one case, *one more carbon atom*, and in the other, *one less carbon atom*, than the aldose with which we started. That is they are *general reactions for increasing and decreasing the carbon content* of aldose sugars. The reactions apply *only to aldoses*. The reaction with hydrogen cyanide by means of which we can pass to the sugar containing one more carbon atom, takes place in the following steps. The hydrogen cyanide first forms the ordinary aldehyde addition compound, viz., the cyan-hydrine or acid nitrile. This acid nitrile, by hydrolysis yields an acid which contains *one more carbon* than the original sugar. Thus far the reaction has already been referred to in connection with the proof that the carbon chain in carbohydrates is a normal chain (p. 322). Now by the reduction of this carbon richer acid the carboxyl group is reduced to the aldehyde group and the result is an aldose sugar containing *one more carbon* than the original sugar.



Decreasing Carbon Content of Aldoses.—The reaction of **hydroxyl amine** with aldose sugars is, in its result, the reverse of the hydrogen

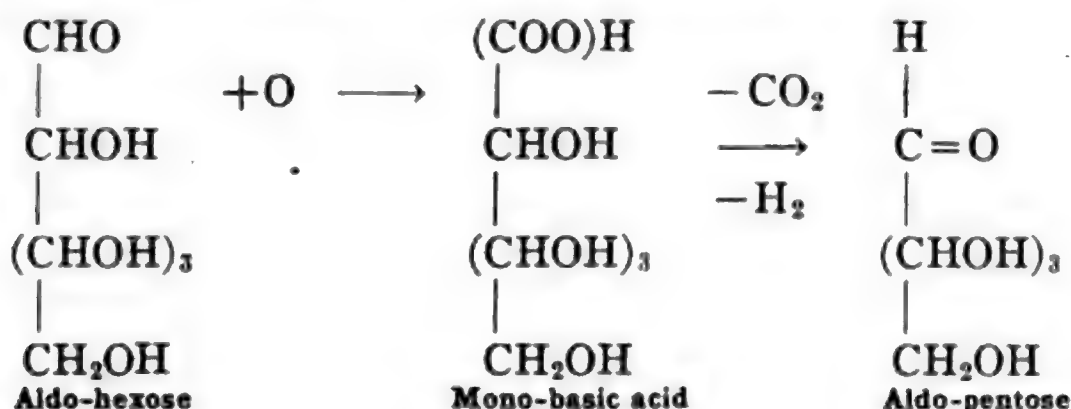
cyanide reaction, *i.e.*, it is a general reaction for *decreasing the carbon content of aldose sugars*. The series of reactions takes place in the following manner. The hydroxyl amine forms, first, the oxime, as has been previously explained, by reacting with the aldehyde group of the aldose. The oximes, by loss of water, are converted into cyanogen compounds, *i.e.*, acid nitriles. When the acid nitriles are treated with ammoniacal silver solution the cyanogen group is split off together with a hydrogen from the neighboring secondary alcohol group. The final product is thus an *aldose containing one less carbon* than the aldose with which we started.



✓ In practice, these reactions do not take place quite as simply as represented above. After the formation of the oxime the compound is acetylated and the conversion into the acid nitrile and into the aldehyde occurs with these acetyl derivatives. The resulting acetyl derivative of the aldo-hexose is first converted into an acetamide compound which on hydrolysis yields the hydroxyl compound, *i.e.*, the aldo-hexose.

The decrease in the carbon content of aldose sugars may also be accomplished by another series of reactions. When the aldose is oxidized with mild oxidizing agents, the product is a mono-basic acid, containing the same number of carbon atoms. When this hydroxy mono-basic acid is treated with hydrogen peroxide, in the presence of ferric acetate, a second oxidation takes place, by which the secondary

alcohol group next to the carboxyl is oxidized to carbonyl, while, at the same time, the carboxyl loses carbon dioxide. This results in the loss of one carbon atom from the original aldose and the formation of a new aldehyde group from the new end primary alcohol.



Reactions of Carbohydrates

Fermentation.—Two general reactions of carbohydrates, are of importance not because the products are direct derivatives of the carbohydrates, but for the commercial value of the product itself, or for the analytical use to which the reaction may be put.

The first general reaction includes several that are embraced in the term *fermentations*. Certain of the carbohydrates, when acted upon by definite micro-organisms (molds, fungi or bacteria), undergo decomposition and the result is definite in each case. We have referred to the formation of lactic acid by the action of certain bacteria upon milk sugar or upon cane sugar. We have, also, in connection with the subject of alcoholic fermentation, in which glucose is decomposed by the enzyme, *zymase*, which is secreted by the yeast plant, discussed sugar fermentation in so far as this particular process and the products of it are concerned. This fermentation is represented by the reaction,



So far as the sugars themselves are concerned, it is interesting, that, they possess very distinct and definite characters in their relation to the yeast enzyme, *zymase*. Of the simple sugars it is only those containing *three, six or nine* carbon atoms, *i.e.*, $\text{C}_3\text{H}_6\text{O}_3$, $\text{C}_6\text{H}_{12}\text{O}_6$, $\text{C}_9\text{H}_{18}\text{O}_9$, which are able to be fermented by this particular enzyme. Furthermore the different six carbon sugars, or hexoses, which we shall presently consider in detail, possess considerable difference as to the ease of fermen-

tation. It has also been shown, by **Emil Fischer**, that the relation of sugars to enzyme action is closely connected with the stereo-chemical configuration of the sugar molecule. The bacterial fermentation of sugars is of an entirely different type from that of the alcoholic fermentation due to zymase. The products of this latter class of fermentations are chiefly acids, especially **lactic, butyric, acetic and carbonic**. In some cases alcohol may be formed and also poly-hydroxy alcohols and gum-like substances. Special fermentations of importance will be considered under each sugar as it is described later.

Reduction of Fehling's Solution.—The reaction of sugars with an alkaline tartrate solution of copper sulphate, known as, **Fehling's solution**, while not giving any information as to the constitution of sugars, is of importance in distinguishing certain sugars and other carbohydrates, and of still more value as the basis of analytical methods for their quantitative determination.

Fehling's solution is an empirical solution, usually made as follows:

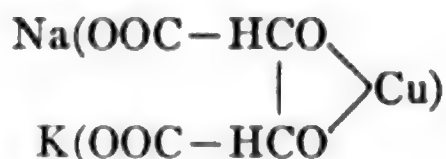
Solution A. Copper sulphate, $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ — 69.30 gm. per liter.

Solution B. Potassium hydroxide, KOH — 250 gm. per liter.

Sodium-potassium tartrate, — 346 gm. per liter.

Rochelle salt.

The following compound is believed to be present.



In this salt the copper is not the *cation* but is part of the *anion* and, therefore, is not precipitated by the alkali as copper hydroxide.

The two solutions, A and B, are kept separate and when used are mixed in equal volumes. Several modifications of the solution have been suggested. **Benedict** uses 200 gm. of anhydrous sodium carbonate instead of potassium hydroxide, and also, substitutes for the Rochelle salt the following mixture:

Potassium citrate — 400 gm.

Potassium thio-cyanate — 250 gm.

Potassium ferro-cyanide — 0.5 gm.

These modifications give a solution especially designed for the determination of small amounts of sugar as it is found in human urine. The modified solution also has the advantage that it can be kept in the mixed condition. The reaction of sugars with **Fehling's solution** consists in the reduction, by the sugar, of the *cupric* copper of the solution with the precipitation of red insoluble cuprous oxide, Cu_2O . The method, as applied in analysis, is wholly empirical, and rests upon the previous accurate determination of the exact amount of cuprous oxide precipitated by definite amounts of pure sugars when solutions of them, of approximate concentrations, are boiled for a definite time under definite conditions. These definite determinations have been made for each one of several sugars and the results have been tabulated and are used in all subsequent determinations.

In addition to its quantitative application Fehling's solution serves as a qualitative test for certain sugars. As will be given under each of the different sugars certain ones have the property of reducing Fehling's solution while others do not. When used as a qualitative test a small amount of Fehling's solution is mixed with a small amount of the supposed sugar solution and then boiled. The appearance of a red precipitate of cuprous oxide proves the presence of some sugar possessing the property of *reducing Fehling's solution*. The property of reducing Fehling's solution, in the case of sugars, probably rests in the presence of the aldehyde or ketone group in the molecule. The products of this reaction, so far as the sugar itself is concerned, are probably unknown.

Chemical Classification of Carbohydrates

We have already developed several facts in regard to the chemical classification and nomenclature of those carbohydrates which are sugars. These facts may be summarized as follows:

1. The termination *ose*, is given to all carbohydrate classes and to those individuals which have sugar character, *e.g.*, *monosaccharoses*, **glycerose**, **glucose**, etc.
2. The numerical prefixes, *bi-*, *tri-*, *tetra-*, etc., are used to indicate the number of carbon atoms in the molecule, *e.g.*, $\text{C}_3\text{H}_6\text{O}_3$ —*Tri-ose*, $\text{C}_6\text{H}_{12}\text{O}_6$ —*Hexose*.
3. Each of the different groups of simple sugars, from tri-oses to non-oses, exists in *two structurally isomeric forms*: (a) that of a poly-hydroxy aldehyde, and (b) that of a poly-hydroxy ketone. To dis-

tinguish between these two forms we use, for the former, the name *aldose*, and for the latter, the name *ketose*. Thus we may have,

an *aldo-pentose* and a *keto-pentose*,
an *aldo-hexose* and a *keto-hexose*, etc.

Mono-saccharoses.—The carbohydrates, or saccharoses, then, are divided into two large classes, viz., *mono-saccharoses* and *poly-saccharoses*.

I. *Mono-saccharoses* are simple sugars which are *not able to be split* by hydrolysis into any simpler sugars, hence the name which signifies *unit* sugars. They have the general formula, $C_nH_{2n}O_n$, and they range in composition from *bi-oses*, containing *two* carbon atoms, to *non-oses* containing *nine* carbon atoms. Each one also with the exception of the bi-oses is known both as an aldose and a ketose.

<i>Bioses</i>	$C_2H_4O_2$	
<i>Trioses</i>	$C_3H_6O_3$	(<i>Aldose + Ketose</i>)
<i>Tetroses</i>	$C_4H_8O_4$	<i>Aldose and Ketose</i>
<i>Pentoses</i>	$C_5H_{10}O_5$	<i>Aldose and Ketose</i>
<i>Hexoses</i>	$C_6H_{12}O_6$	<i>Aldose and Ketose</i>
<i>Heptoses</i>	$C_7H_{14}O_7$	<i>Aldose and Ketose</i>
<i>Octoses</i>	$C_8H_{16}O_8$	<i>Aldose and Ketose</i>
<i>Nonoses</i>	$C_9H_{18}O_9$	<i>Aldose and Ketose</i>

Poly-saccharoses.—(II) *Poly-saccharoses*, as the name indicates, are not simple sugars, but are multiples of the unit sugars. On hydrolysis, they *split into two or more molecules* of one of the simple sugars, or mono-saccharoses. This class is further sub-divided into two sub-classes due to the fact that some of them are compounds possessing true sugar characters, while others are not true sugars.

(II_a) *Poly-saccharoses* that are *true sugars*. The members of this sub-class consist of two groups, only one of which is of great importance.

Di-saccharoses or Hexo-bioses.—(I) The first group is known as *di-saccharoses*. These are so called because they split, on hydrolysis, into *two* molecules of hexose mono-saccharoses. The general formula for these di-saccharoses is $C_nH_{2n-2}O_{n-1}$, and the known members all have the composition formula $C_{12}H_{22}O_{11}$. They are represented by such common substances as **cane sugar**, **milk sugar** and **malt sugar**. The reaction of hydrolysis is,



On this account they are also called hexo-bioses, which term is somewhat confusing because of the different meaning given to the word bi-oses.

Tri-saccharoses or Hexo-trioses.—(2) The other less important group of the poly-saccharoses that are true sugars is that of the *tri-saccharoses*, or hexo-trioses. These split, as their name indicates, into *three* molecules of hexose mono-saccharoses. The formula corresponds to the composition $C_{18}H_{32}O_{16}$. The hydrolysis may be represented by the reaction,



Poly-saccharoses not True Sugars.—(II_b) The second-sub-class of poly-saccharoses consists of those carbohydrates which are *not true sugars*. This group is represented by such substances as **starch, dextrin and cellulose**. The group is usually known by the simple name, poly-saccharoses, as the specific names, di-saccharoses and tri-saccharoses, are used for the members of the first subclass. We do not know how many molecules of mono-saccharoses are obtained from one molecule of these poly-saccharoses, because we do not know the molecular weight of the compounds. They are represented by the empirical formula $(C_6H_{10}O_5)_x$, and their hydrolysis may be represented as follows:



Summarizing our classification of the carbohydrates we have,

(I) *Mono-saccharoses, aldoses and ketoses.*

$C_2H_4O_2$, *Bioses* to $C_9H_{18}O_9$, *Nonoses*

These do not hydrolyze to any simpler sugars.

(II) *Poly-saccharoses.*

(a) *True Sugars.*

(1) *Di-saccharoses, or Hexo-bioses,*



These hydrolyze to two molecules of mono-saccharoses, $C_6H_{12}O_6$.

(2) *Tri-saccharoses, or Hexo-trioses,*



These hydrolyze to $3C_6H_{12}O_6$.

(b) *Not true sugars.*

Poly-saccharoses, $(C_6H_{10}O_5)_x$.

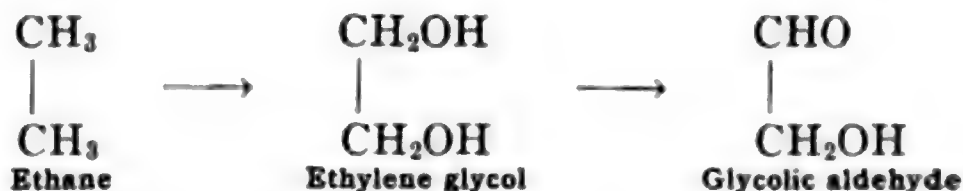
These hydrolyze to $xC_6H_{12}O_6$.

Having thus established our system of classification of the carbohydrates as based upon their constitution, we are now ready to take up the various individual members and study them as to their occurrence, general properties, and commercial uses. Also as to their specific relation to each other and special points in regard to their constitution.

A. MONO-SACCHAROSES. $C_nH_{2n}O_n$

I. BIOSES. $C_2H_4O_2$

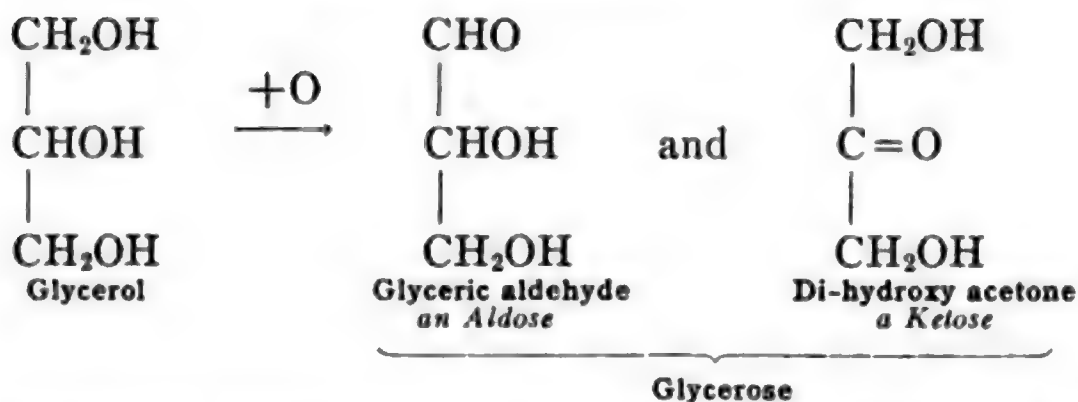
Plainly, the simplest compound which contains both alcohol and aldehyde groups is the compound derived from ethane by the oxidation of one of the methyl groups to alcohol and the other to aldehyde, or from ethylene glycol by the oxidation of one of the alcohol groups to aldehyde, viz.,



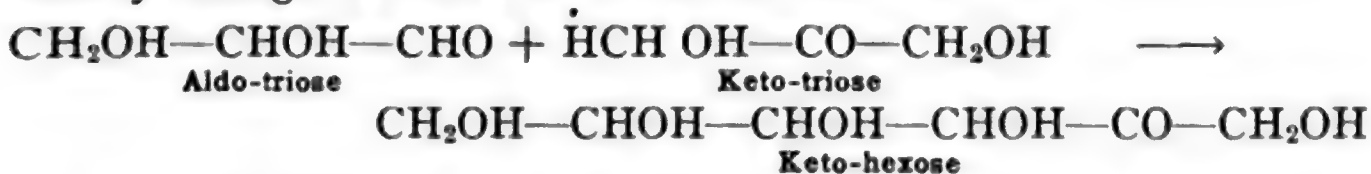
This compound has already been mentioned and is known as glycolic aldehyde. According to our system of classification and of naming the carbohydrates this compound would be a biose, or a two carbon sugar. Glycolic aldehyde does not, however, possess the general characters of a sugar and though it is truly the simplest representative of the carbohydrates it is not usually included as such.

II. TRIOSSES. $C_3H_6O_3$

The alcohol-aldehyde compound containing three carbon atoms, *i.e.*, a *triose*, has also been referred to (p. 229). It is the compound usually regarded as the simplest sugar. While the biose, just referred to, cannot exist as a ketone-alcohol compound, the triose can exist both as the aldehyde alcohol and also as the ketone alcohol compound. It is obtained, as has been previously stated, by the oxidation of the three carbon tri-hydroxy alcohol, glycerol. On this account it has been given the name of **glycerose**. The substance known as glycerose is not an individual compound of the aldehyde or ketone constitution, but is a *mixture of both of these compounds*, as they are formed by the oxidation of glycerol.



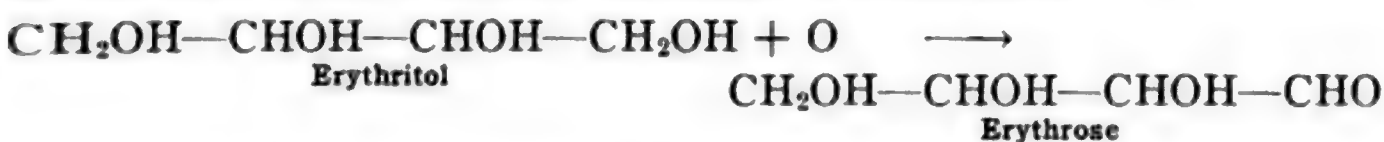
The oxidation of glycerol may be accomplished by means of several reagents, *e.g.*, dilute nitric acid, bromine, bromine and sodium carbonate, platinum black, etc. The best method, in practice, is to oxidize the lead salt of glycerol by means of bromine vapor. By such oxidation it is mostly the ketone compound which is formed, though the aldehyde is always present. As obtained, glycerose is a sweet syrup which readily reduces Fehling's solution, reacts with phenyl hydrazine, forming osazones, and is fermentable by yeast zymase yielding alcohol. The most important fact in connection with glycerose is that it *polymerizes* easily, under the influence of alkalies, and yields a *keto-hexose*. This polymerization takes place by a condensation exactly analogous to the *aldol condensation*.



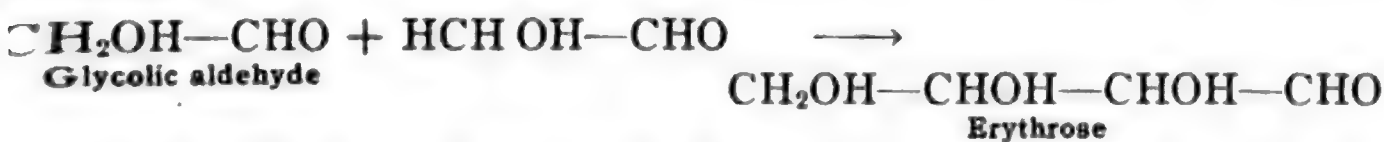
We shall consider this condensation again when we consider the hexose sugars.

III. TETROSES. $\text{C}_4\text{H}_8\text{O}_4$

A tetrose, known as **erythrose**, has been obtained by the oxidation of the tetra-hydroxy alcohol, **erythritol**, or *butan-tetrol*.

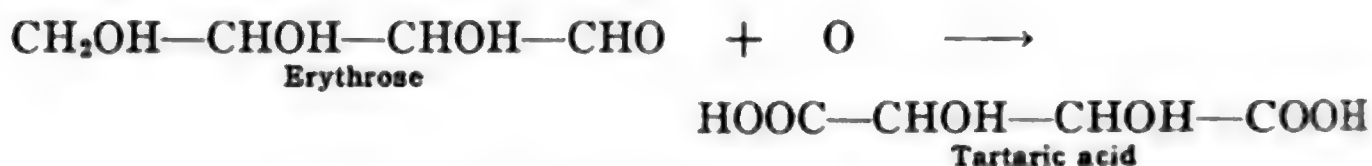


It has also been prepared by the aldol condensation of glycolic aldehyde,



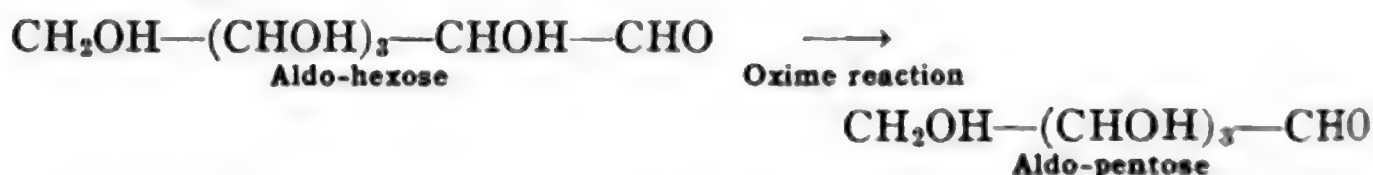
Erythrose yields an osazone with phenyl hydrazine and reduces **Fehling's solution** but is *not fermentable with yeast zymase*. When

oxidized, by strong oxidizing agents, to a di-basic acid it yields **tartaric acid**.

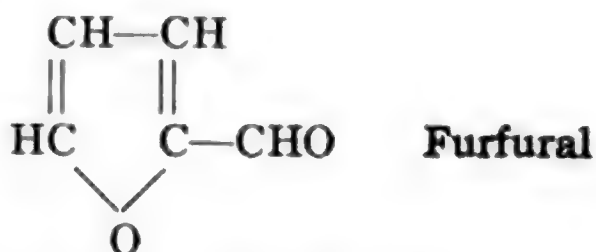


IV. PENTOSES. $\text{C}_5\text{H}_{10}\text{O}_5$

Pentose sugars may be obtained by the oxidation of the normal pentahydroxy alcohol. The usual method of preparing them, however, is by decreasing the carbon content of a hexose sugar by means of the oxime reaction (p. 330).



Pentosans.—The importance of the pentose sugars lies in their wide distribution, in nature, in the **pectins** and gummy substances of many plants. The chief sources of two of the pentose sugars are *gum Arabic* and *wood gum*. In the *pectins* and other substances of plants the pentoses do not, probably, occur free, but in the form of complex substances known as **pentosans**. When these pentosans are boiled with acid, hydrolysis takes place and the pentose is set free. The pentosans therefore bear the same relation to pentoses that the polysaccharoses do to the hexoses, *i.e.*, they are *polypentoses*. When a pentose sugar is heated with strong hydrochloric acid and distilled, it is decomposed and yields **furfural** which distils over. Furfural is a *cyclic compound*, to be considered later (Pt. II), to which the following formula has been given,

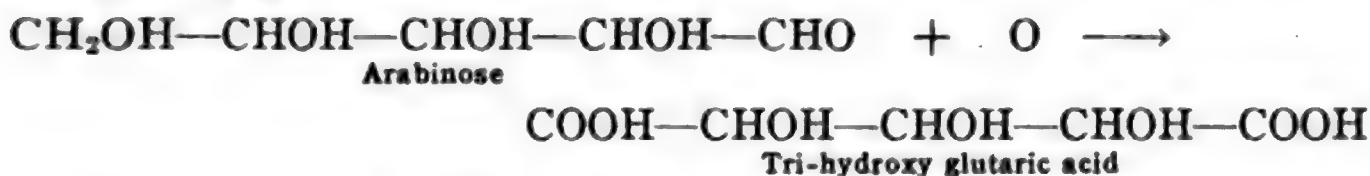


When an acid solution of **phloroglucinol** (Pt. II) is added to furfural a black precipitate, known as a **phloroglucid**, is formed. From the weight of this phloroglucid we may calculate, by empirical methods, the amount of furfural and, from this, the amount of pentose sugar with which we started, or also, the amount of pentosan. This is the basis of the analytical method for the determination of pentosan compounds in plant materials. As the pentosans possess considerable nutritive

value as foods, especially in stock feeds, their determination is of importance.

Ariabnose, $\text{CH}_2\text{OH}-(\text{CHOH})_3-\text{CHO}$

This sugar is an aldo-pentose, and is obtained, synthetically, by degrading a certain stereo-isomeric hexose sugar known as **mannose**. It may also be obtained, as the name indicates, and as has been stated above, by hydrolyzing gum Arabic or cherry gum. It is crystalline and melts at about 160° . It has a sweet taste and is optically active, being dextro rotatory. It forms an osazone which melts at $157^\circ-158^\circ$. By reduction it yields **arabitol**, a penta-hydroxy alcohol. On oxidation with strong oxidizing agents it yields a di-basic acid, viz., **tri-hydroxy glutaric acid**,



Xylose, $\text{CH}_2\text{OH}-(\text{CHOH})_3-\text{CHO}$

This sugar is also an aldo-pentose and is stereo-isomeric with arabinose. It is known as *wood sugar* because it is obtained by the hydrolysis of wood gum, i.e., of the pentosans present in this gum. It is crystalline and melts at $140^\circ-160^\circ$. It is optically active, being dextro-rotatory. Its osazone melts at 160° . By reduction it yields a penta-hydroxy alcohol and by oxidation it yields tri-hydroxy glutaric acid.

Rhamnose, $\text{C}_6\text{H}_{12}\text{O}_6$, $\text{CH}_2-\text{CHOH}-(\text{CHOH})_3-\text{CHO}$

As will be seen from the above formula, rhamnose is an example of a carbohydrate in which the hydrogen and oxygen are not in the proportion of H_2O . It has been proven to have the constitution of a *methyl substitution product* of a pentose sugar. It is obtained by the hydrolysis of certain glucosides. It is crystalline and the crystals contain one molecule of water. The anhydrous sugar melts at 93° . It tastes sweet, is dextro rotatory and its osazone melts at 180° .

V. HEXOSES. $\text{C}_6\text{H}_{12}\text{O}_6$

Synthesis from Poly-alcohols.—We come, now, to that group of mono-saccharoses, the **hexose mono-saccharoses**, which contains the most important simple sugars which are known, viz., **glucose** and **fructose**. The hexoses may be prepared, synthetically, by oxidizing the hexa-hydroxy alcohols, e.g., **mannitol**, **dulcitol**, **sorbitol**, etc. (p. 219).

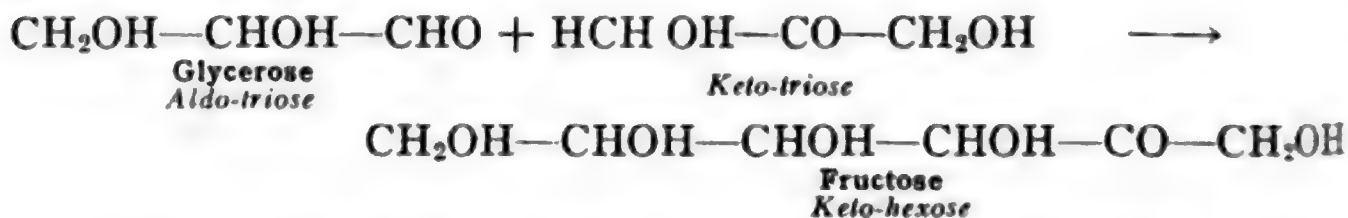
Naturally occurring substances are known in the two structural forms of aldo-hexoses and keto-hexoses.

Glucose, $\text{CH}_2\text{OH}-\text{CHOH}-\text{CHOH}-\text{CHOH}-\text{CHOH}-\text{CHO}$,
Aldo-hexose.

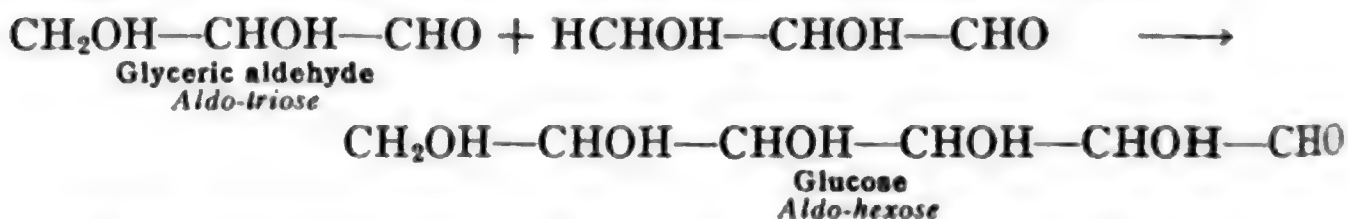
Fructose, $\text{CH}_2\text{OH}-\text{CHOH}-\text{CHOH}-\text{CHOH}-\text{CO}-\text{CH}_2\text{OH}$,
Keto-hexose.

The aldo-hexose is the commonly known and widely distributed substance **glucose** or grape sugar, The keto-hexose is also widely distributed but less commonly known. It is called **fructose** or fruit sugar. The constitution of these two sugars, glucose as an *aldo-hexose* and fructose as a *keto-hexose* has been proven by the reactions already discussed as proving the position of the aldehyde and the ketone group (p. 322).

From Glycerose.—A second synthesis of hexoses is the aldol condensation of glycerose, as already referred to (p. 337). As glycerose is a mixture of the two compounds, **glyceric aldehyde** (*aldo triose*), and **di-hydroxy acetone** (*keto-triose*), the condensation product is the *keto-hexose*, or **fructose**.

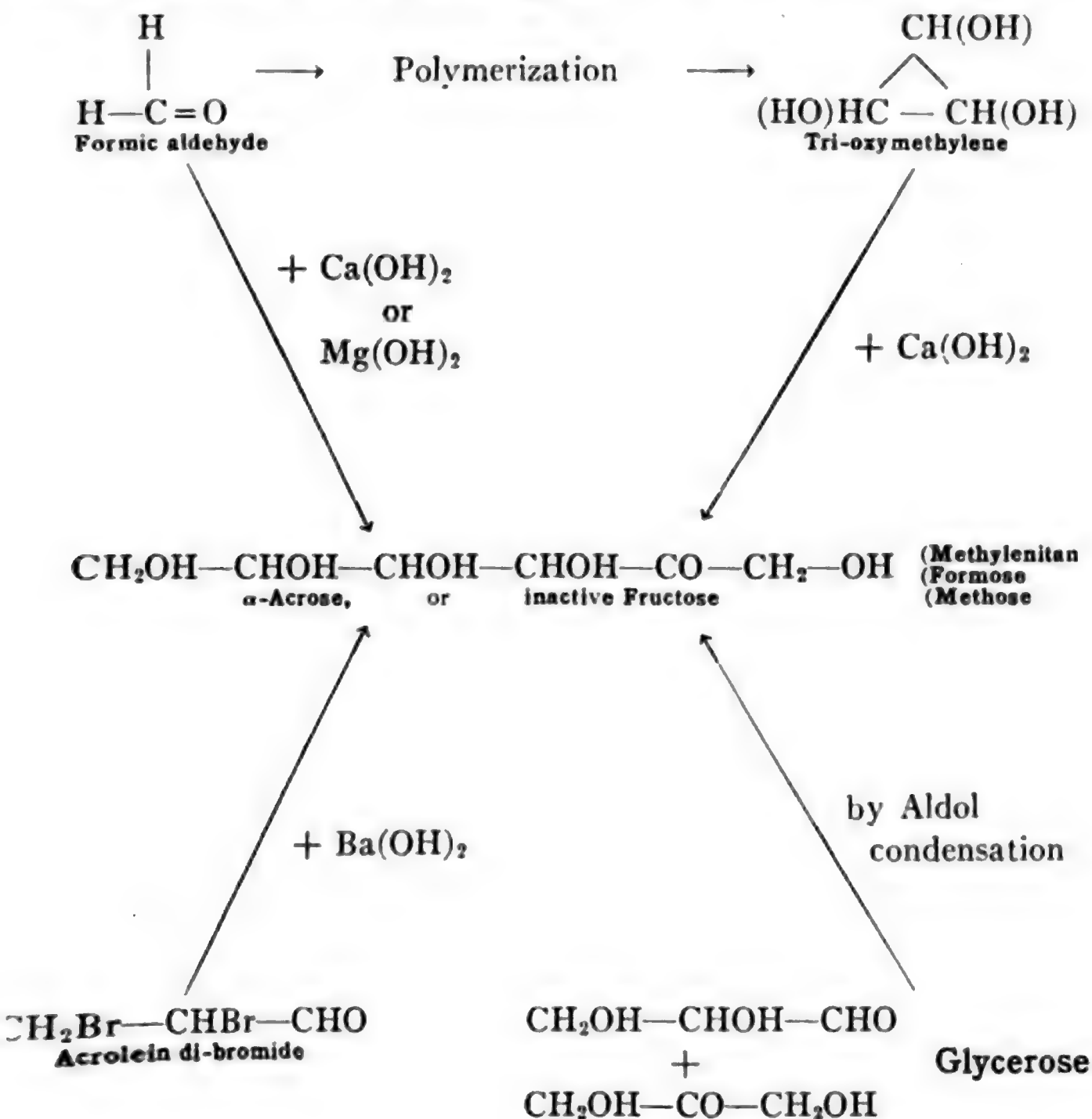


If, instead of condensing glycerose, we condense the aldo-triose, **glyceric aldehyde**, by itself, we then obtain the aldo-hexose, or **glucose**.



From Formaldehyde.—Historically and physiologically, the most important synthesis of hexose mono-saccharoses is from **formaldehyde**. In 1861 **Butlerow** found that **dioxymethylene** (**tri-oxymethylene**), produced by polymerizing formaldehyde, yielded with hot lime water a sweet substance to which he gave the name of **methylenitan**. The substance reduced Fehling's solution, but was optically inactive and non-fermentable with yeast zymase. Later, **Loew** obtained a sweet, non-fermentable syrup by the direct action of lime-water on formaldehyde. This substance he called **formose**. He afterward obtained what he considered another sugar by the action of magnesium hydroxide upon formaldehyde. This substance was fermentable by yeast and to it he gave the name of **methose**. In 1887, **Fischer and Tafel**

obtained, by the action of barium hydroxide upon **acrolein di-bromide**, and also by the condensation of **glycerose**, by means of alkalis (p. 337), a sugar which they called, α -**acrose**, and which they showed was identical with **inactive fructose**. They also showed that the three substances just mentioned, prepared by **Butlerow** and **Loew** were, probably identical with this new one. This was the first time that a hexose mono-saccharose had ever been synthesized and the importance of this work can hardly be realized. As we shall discuss later, the synthesis of hexose sugars from formaldehyde is of fundamental importance in connection with the process of photo-synthesis in the leaves of green plants. We may summarize the synthetic reactions above mentioned in the following way.



Hydrolysis of Poly-saccharoses.—The most important relationship of the hexose sugars is that involved in the common method for their preparation. **Poly-saccharoses**, *e.g.*, cane sugar and starch, *hydrolyze and split into two or more molecules of hexose sugars*. On the hydrolysis of a di-saccharose *two* molecules of hexose sugars result. These two molecules may be the same hexose sugar or they may be different. When a true poly-saccharose, like starch, is hydrolyzed *more than two* molecules of hexose sugar result. These hydrolytic reactions will be considered in detail under the different poly-saccharoses.

Stereo-isomerism of the Mono-saccharoses

It will be necessary, now, to consider the *stereo-isomerism* of those mono-saccharoses which contain more than three carbon atoms. The isomerism of the aldoses and ketoses is structural, depending upon the different groups present in the molecule. These two isomeric forms of the mono-saccharoses are found in the case of each member above the bi-ose group, as this can exist only in the condition of an aldehyde compound and not as a ketone. If we examine the structural formula of any mono-saccharose containing more than three carbons we shall find that they each contain at least one *asymmetric carbon atom*. In most cases two or more asymmetric carbons are present, as shown in the following formulas in which the asymmetric carbon atoms are marked.



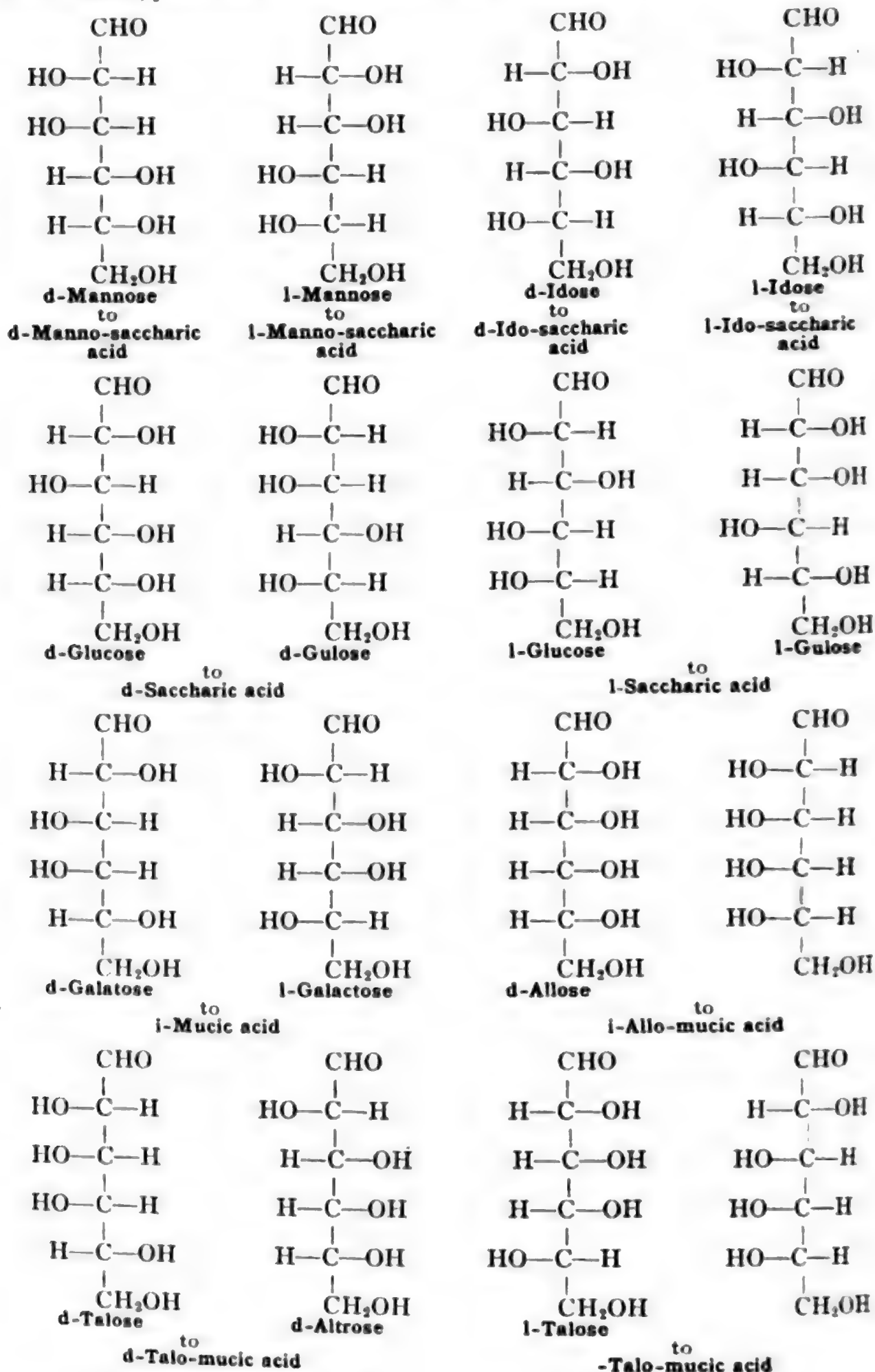
In the case of glyceric aldehyde we also have an asymmetric carbon and should have stereo-isomerism, but in the case of this compound such isomers are unknown. In the following discussion we shall use only the hexose sugars and the aldose form of these. A fuller discussion of the stereo-isomerism of these compounds, involving all compounds, will be found in larger books, such as **Cohen**, and **Meyer and Jacobson**.

Number of Stereo-isomers.—Plainly, with more than one asymmetric carbon atom in the molecule, we can have *more than two* stereo-isomers, as we had in the case of lactic acid. When we speak of the number of stereo-isomers we do not include the racemic form as it

is made up of the two optical isomers. Thus in lactic acid we say there are two stereo-isomers and in tartaric acid there are three. In the latter case we include the meso-tartaric acid as it is an unresolvable inactive form. Nor do we mean that the stereo-isomers all possess different optical activity, as here, of course we can have only two forms, viz., the *dextro* and the *levo*. We mean by stereo-isomers any two, or more compounds, in which, considering all the asymmetric carbon atoms present, there is a different space configuration. Two such isomers may, or may not, have the same optical activity, or they may be optically inactive, by intra-molecular compensation.

From a study of stereo-isomerism, **van't Hoff** has developed the following formula as expressing the number of stereo-isomers possible with any number of asymmetric carbon atoms, when the compound is unsymmetrical in that the two halves are *unlike*. If n represents the number of asymmetric carbon atoms in the molecule, then, $A = 2^n$, in which A is the number of stereo-isomers which may be formed. In a compound, like an aldo-hexose, just given, in which there are *four* asymmetric carbon atoms, we have according to the above formula, $n = 4$ therefore $A = 2^4 = 16$. This formula applies only in the case of compounds in which the two halves of the compound are unlike, as with the aldo-hexoses, but not in the case of compounds, like tartaric acid, in which the two halves of the compound are alike. The mono-basic acids resulting from the aldo-hexoses are also unsymmetrical and hold to the **van't Hoff** formula. The dibasic acids and the poly-hydroxy alcohols, resulting from the aldo-hexoses are, however, unsymmetrical only in case they contain an odd number of carbon atoms, *i.e.*, pentose, heptose and nonose derivatives. With the like derivatives of mono-saccharoses containing an even number of carbons, *i.e.*, tetroses, hexoses, and octoses, we have as in tartaric acid, a symmetrical compound in which the two halves of the molecule are alike and in such compounds the formula of **van't Hoff** does not hold. In all compounds of this latter type we have the formation of inactive compounds of the character of meso-tartaric acid. On the next page we give the space configuration of all the sixteen possible stereo-isomers of the aldo-hexose sugar, viz., $\text{CH}_2\text{OH}-\text{CHOH}-\text{CHOH}-\text{CHOH}-\text{CHOH}-\text{CHO}$, $\text{C}_6\text{H}_{12}\text{O}_6$, the commonly occurring form of which is the well known **glucose** or grape-sugar. The dibasic acid obtained from each isomer is also indicated. It is a striking confirmation of the

theories of stereo-chemistry that, of the possible *sixteen* stereo-isomeric aldo-hexoses, *fourteen* are known at the present time.



It would be out of place, in this book, to discuss in detail the methods by which a definite configuration has been assigned to each known aldohexose and, similarly, to each known stereo-isomer of the tetrose, pentose and heptose groups. We may form some idea of how it is accomplished by recalling the following transformations that are possible in the case of any aldose mono-saccharose. (1) *By oxidation*, we may pass to the corresponding mono-basic and di-basic acids, as indicated in the table of isomers on the preceding page; (2) *by reduction*, to the poly-hydroxy alcohols; (3) *by the osazones and osones*, from an aldose to its corresponding ketose; (4) *by the hydrogen cyanide reaction*, to the aldose sugar containing one more carbon atom; and, finally, (5) *by the oxime reaction*, to the aldose sugar containing one less carbon atom. By means of all of these reactions combined it has been possible to show definitely the relationship in configuration between all known sugars of whatever carbon content whether aldose or ketose in structure.

It must be emphasized, that the designations *d-*, *dextro* and *l-*, *levo* for the stereo-isomers, refers wholly to their *configuration in space* and has *no reference to the optical activity*, so far as the direction of the rotation is concerned, for this may be the same or different. This is illustrated by the fact that **d-glucose**, which itself is *dextro rotatory*, by means of its osazone and osone, is converted into the corresponding ketose sugar which, therefore, must be the *dextro* form of fructose. It is, however, *levo* in the direction of its optical rotation, *i.e.*, **d-fructose** is *levo-rotatory*.

Lactone Constitution of Glucose

In discussing the aldehyde and ketone constitution of the mono-saccharoses we stated that while this constitution holds for the compounds as they react *in water solution* it is not the constitution at present accepted for the actual substances themselves.

Muta-rotation.—Two facts have led to an advancement in our ideas as to the constitution of the carbohydrates, especially of glucose. The first fact is that a solution of glucose changes in its optical rotatory power, being nearly twice as great when the solution is freshly prepared as it is when the solution has stood for some time. This changing of rotatory power has been termed *muta-rotation*. The muta-rotation of glucose has been understood only in connection with a constitution which makes possible the existence of two isomeric forms possessing

different rotatory power and which exist together under a changing condition of equilibrium.

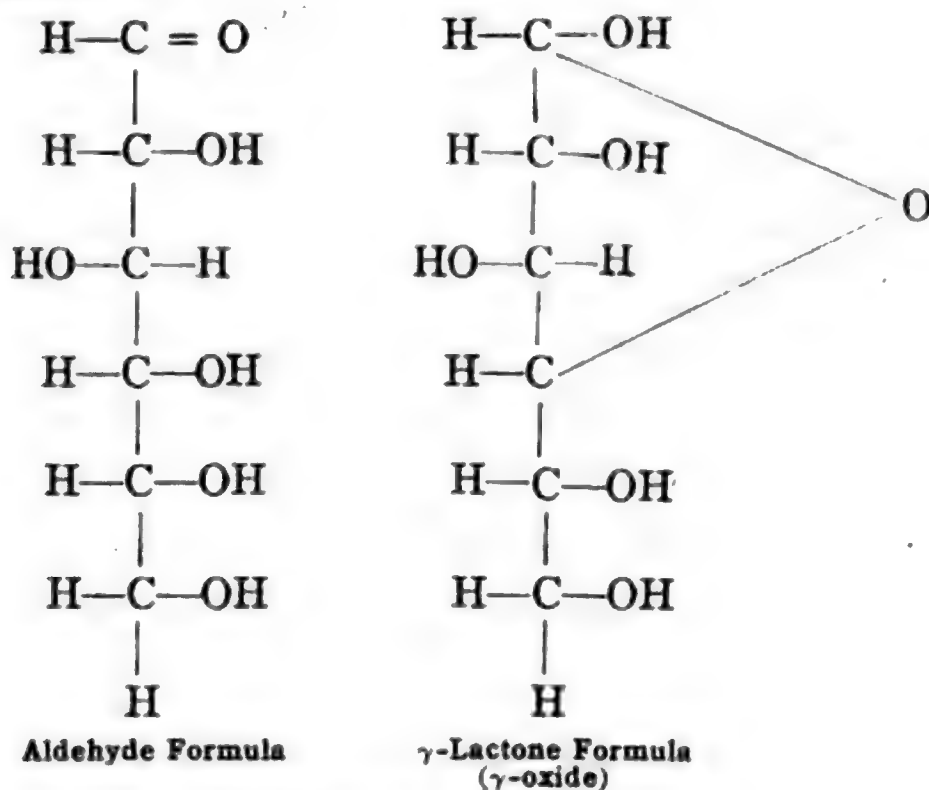
Alpha- and Beta-Methyl Glucosides.—The second fact which brought about a change in our ideas as to the constitution of glucose is that there have been shown to exist two isomeric methyl ethers derived from **d-glucose**. We have spoken of only one class of derivatives of the mono-saccharoses, viz., the esters resulting from the reaction of the alcoholic hydroxyl groups with an acid chloride or acid anhydride. As alcohols, however, the mono-saccharoses form both potassium salts or alcoholates analogous to potassium ethylate, C_2H_5OK , and they also form ethers analogous to methyl or ethyl ether. When glucose (d-glucose) is dissolved in methyl alcohol and the solution treated with dry hydrochloric acid gas a methyl ether of glucose is formed. This methyl ether which is known as **methyl glucoside** exists in two isomeric forms distinguished as **α -methyl glucoside** and **β -methyl glucoside**. They were discovered by **Emil Fischer** in 1893 and are considered analogous to the natural glucosides.

Alpha and Beta Glucoses.—From the two isomeric methyl glucosides **Armstrong** obtained two isomeric glucoses. **α -Methyl glucoside** is hydrolyzed by the action of the enzyme maltase and when so hydrolyzed **α -glucose** is obtained. Similarly **β -methyl glucoside** hydrolyzed by **emulsin** yields **β -glucose**. The two isomeric forms of glucose are readily transformed into each other and exist together in equilibrium but by controlling the conditions each of the forms has been obtained and studied. The methyl glucosides differ from glucose in *not* reacting with either Fehling's solution or with phenyl hydrazine and in *not* exhibiting muta-rotation. The optical rotation of the glucosides and the glucoses is as follows:

α -Methyl glucoside, m. p. 165° (α)_D = $+157^\circ$ **α -Glucose** (α)_D = $+105^\circ$
 β -Methyl glucoside, m. p. 104° (α)_D = -33° **β -Glucose** (α)_D = $+22^\circ$

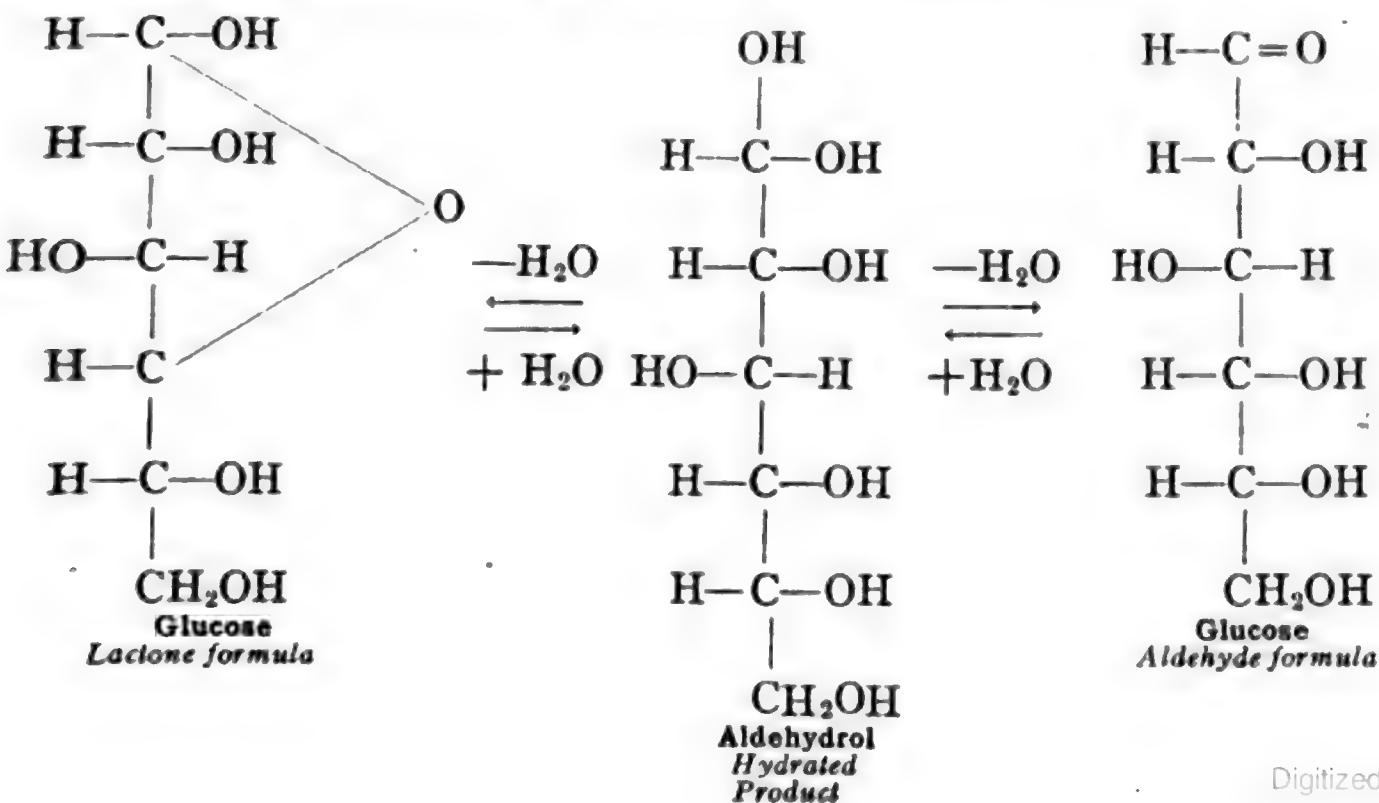
Lactone Formula.—What now is the accepted constitution of these glucosides and of glucose and how does it explain the existence of two isomeric forms of each and also the muta-rotation of glucose? As early as 1883 **Tollens** suggested another constitution than the aldehyde-alcohol one for glucose because the compound is not as reactive as such a constitution would indicate. He suggested that four of the carbon atoms in the hexose chain were linked by an oxygen atom into a ring. If we examine the formula of glucose as given for the aldehyde consti-

tution we see that in any such poly-hydroxy compound there is the possibility of the formation of a *gamma-lactone ring* similar to the *lactones* formed from the *gamma-hydroxy acids* (p. 243). The two formulas are as follows:



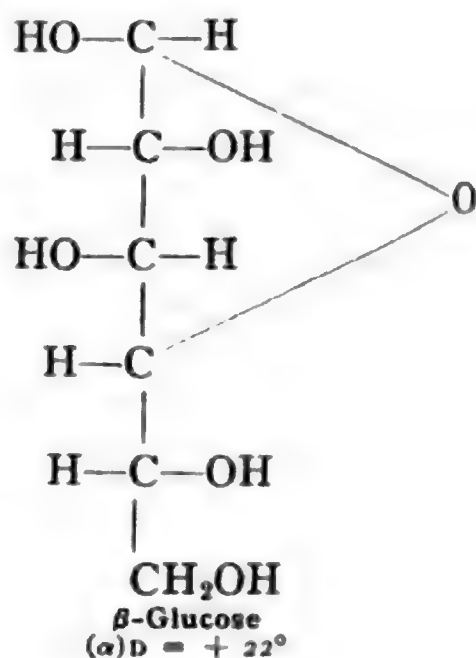
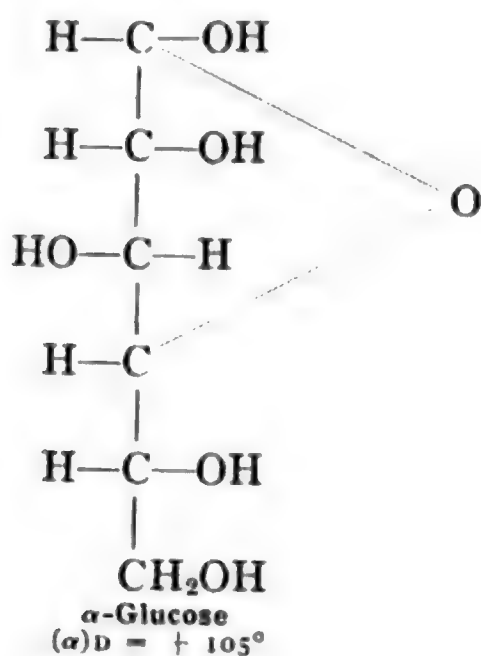
d-Glucose

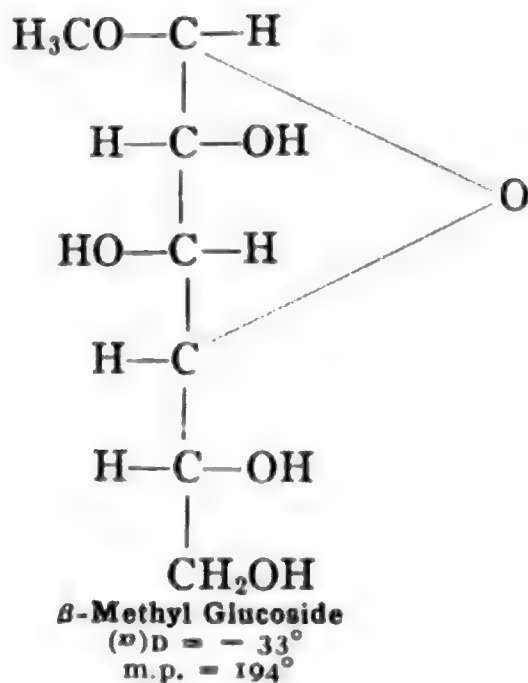
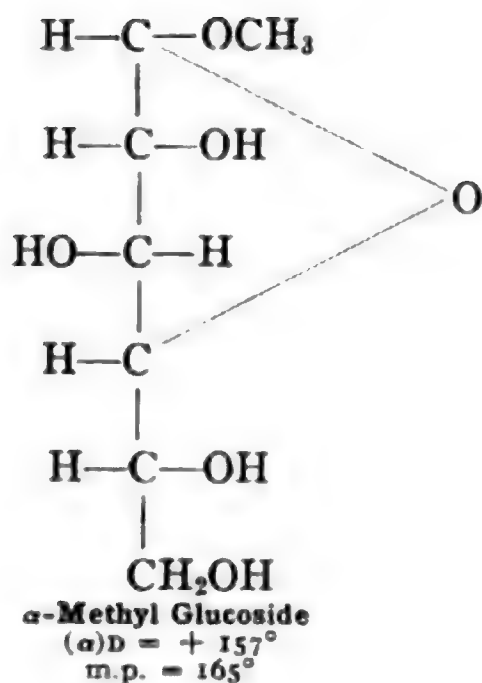
Such a lactone would be the anhydride of a compound containing two hydroxyl groups linked to one carbon atom. A compound of this character would also be able to lose water in another way as discussed in connection with aldehyde (p. 115) yielding a product of the aldehyde constitution as follows:



This explains what takes place when glucose in water solution acts as an aldehyde toward phenyl hydrazine and other reagents. When put into water solution a small amount of the glucose of the lactone constitution is converted into the hydrated produce called **aldehydrol**. Under the influence of the reagent, phenyl hydrazine, the aldehydrol loses water yielding the aldehyde which is then removed by reaction with the reagent. This results in another portion of the lactone being converted into the aldehydrol and this to the aldehyde and so on until all of the glucose is converted into the aldehyde and reacted upon by the phenyl hydrazine. In water solution without the phenyl hydrazine the lactone and the aldehydrol exist in equilibrium the reaction with water being reversible.

Explanation of Isomeric Glucoses and Glucosides.—As the lactone constitution fixes the position of the hydrogen and hydroxyl which are linked to the end carbon atom of the lactone ring stereo-isomerism of the *geometric* type is possible. The two isomeric glucoses and the two isomeric methyl glucosides are thus represented as follows:

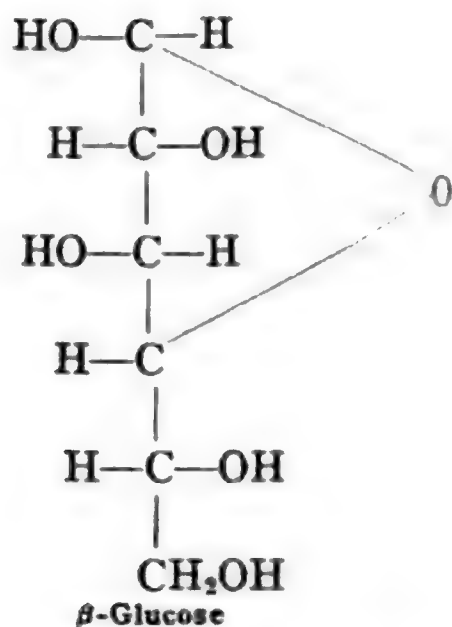
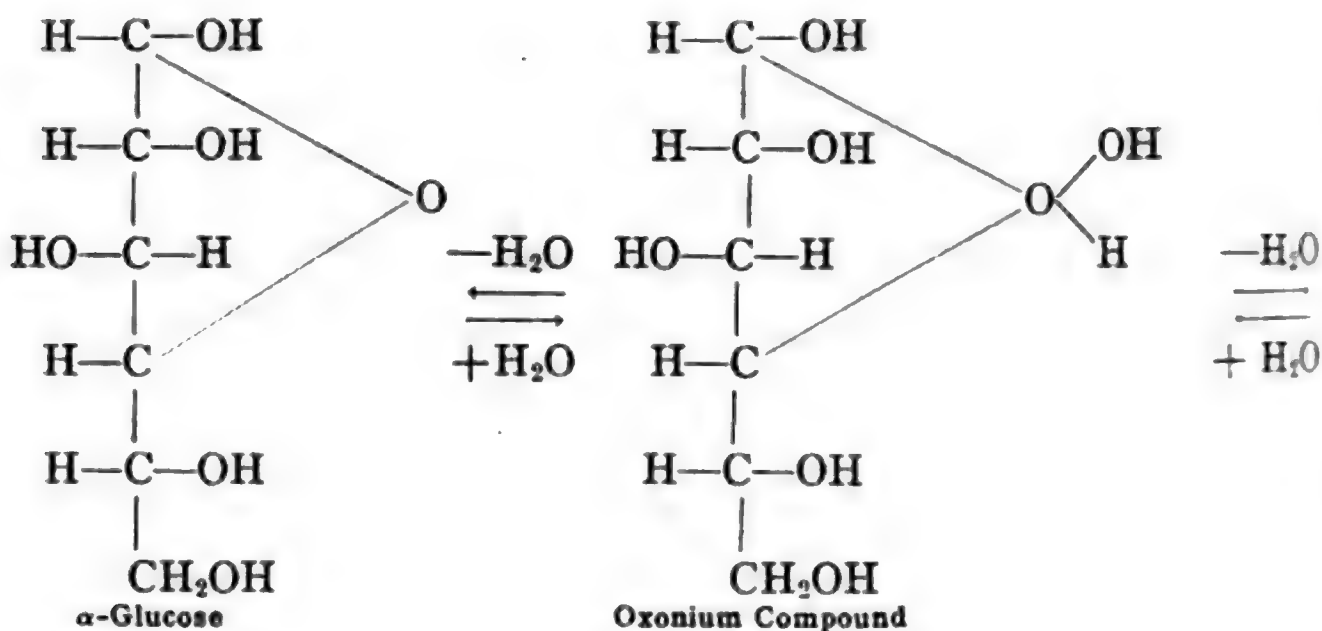




That both of the glucoses and also both of the methyl glucosides have been prepared and their relationship to each other established supports the theory of the lactone constitution.

Explanation of Muta Rotation.—That glucose in water solution undergoes a rapid change in its optical rotation is explained by the easy conversion of the two isomeric glucoses into each other. Starting with (α)-glucose when it goes into solution some hydration occurs and the *aldehydol* is formed. The reaction being reversible glucose is reformed but in reforming the lactone either the *alpha* or the *beta* form is possible and *some beta* results. The formation of the beta isomer effects a change in the optical rotation. This continues until equilibrium is established when the optical rotation remains constant but is different from that which it was at the beginning when the glucose was first dissolved.

Oxonium Compound.—The transformation of *alpha* and *beta* glucoses into each other resulting in muta-rotation has also been explained by **Armstrong** in another way than through the intermediate aldehydol compound. According to this author the hydration of the lactone form of glucose results in the formation of an *oxonium* compound in which oxygen is *tetra-valent*. The loss of water from this oxonium compound restores the lactone constitution but in returning to the lactone *either the alpha or beta form may result*.



In the loss of water from the oxonium compound an unsaturated intermediate product is formed by the hydrogen and hydroxyl being taken one from the oxonium group the other from the carbon atom at the end of the lactone ring. The saturated lactone is then formed from this intermediate unsaturated compound by a *shifting of the oxonium hydrogen atom to the neighboring carbon atom*.

Further details of these transformations of the isomeric glucoses and methyl glucosides and other facts in support of the lactone constitution of glucose must necessarily be omitted from our study though they are essential to a full understanding of the matter. For such fuller discussion such works as **Armstrong** and **Cohen** may be consulted. We may simply add that recent work by **Nef** and his pupils not only supports the lactone constitution but shows that both *alpha-lactones*

and *beta-lactones* as well as *gamma-lactones* are possible in the case of the glucoses.

We may now take up the consideration of the individual carbohydrates following the order of our classification, viz., (1) *Mono-saccharoses*, (2) *Di-saccharoses*, or poly-saccharoses that are *true sugars*, and (3) *Poly-saccharoses*, or poly-saccharoses that are *not true sugars*.

Glucose, Dextrose, Grape Sugar

Of the hexose monosaccharoses only two of the fourteen known aldohexoses need to be described in detail and only one keto-hexose. The most important hexose sugar is **glucose**. As it is also *dextro-rotatory* toward polarized light, it is known as **dextrose**. This sugar is very widely distributed in nature, being found in the juice of most sweet fruits, especially in grapes. On account of this last fact it is known also as **grape-sugar**. The three names, therefore, viz., **glucose**, **dextrose**, and **grape-sugar**, all apply to the same chemical compound. We shall use the name glucose in preference to dextrose except in particular cases. It is also found in certain roots, leaves and flowers and in human urine in the pathological condition known as *diabetes*. It is a normal constituent of human blood where it is present to the amount of 0.1 per cent. It may be prepared by the hydrolysis of starch or cane sugar the former being the commercial source. Corn syrups are made by hydrolyzing corn starch and are composed largely of glucose. Glucose crystallizes from alcohol, or from concentrated water solution, in anhydrous needles which melt at 146° . It also forms crystals with one molecule of water of crystallization. It is easily soluble in water, or in dilute alcohol, but practically insoluble in absolute alcohol. It is optically active, being *dextro* rotatory, $(\alpha)_D = +53^{\circ}$ at 20°C . It *reduces Fehling's solution* and is *fermented by yeast zymase* with the formation of alcohol. Its osazone crystallizes in tufts of thin needles. In its space configuration it is **d-glucose**. The **l-glucose** and the **i-glucose** (racemic form) are also known.

Galactose

The other aldo-hexose which we shall mention is **galactose**. This sugar is stereo-isomeric with d-glucose. The two having the respective configurations as given in the table, p. 344. It is obtained by the

hydrolysis of milk-sugar, or lactose. It crystallizes in microscopic hexahedra which melt at 168° . It *reduces Fehling's solution* and is *fermentable by yeast zymase*. It also yields an osazone.

Fructose, Levulose, Fruit Sugar

The remaining hexose, which we shall mention, is a keto-hexose. It is structurally isomeric with glucose. Because it is found widely distributed in fruits, where it is usually associated with glucose, it is known as **fructose**, and also as **fruit-sugar**. It is found in honey and is also obtained by the hydrolysis of a poly-saccharose known as **inulin** which is found in Dahlia tubers. It is optically active being *levo-rotatory*, the opposite of glucose, $(\alpha)_D = -92^{\circ}$ at 20°C . Because it is levo-rotatory it is also known as **levulose**. The three names, therefore, viz., **fructose**, **levulose** and **fruit-sugar**, correspond to the three similar names for glucose. It is known in the three stereo-chemical forms of *d*-, *l*-, and *i*-, and these three forms are all structurally isomeric with the three similar forms of *d*-glucose. As stated before it corresponds, in configuration to **d-glucose** and is therefore stereo-chemically **d-fructose**. When glycerose is condensed, or polymerized, to a hexose sugar, it is the **i-fructose**, also known as **α -acrose**, which is formed. This was the first hexose sugar to be prepared synthetically. Fructose crystallizes with difficulty from alcohol in water free crystals. From water it crystallizes with $\frac{1}{2}$ molecule of water of crystallization. It *reduces Fehling's solution* and undergoes alcoholic *fermentation with yeast zymase*. It yields the *same osazone as glucose*.

Invert Sugar. Inversion.—We have mentioned the fact that glucose may be obtained by the hydrolysis of cane-sugar. In this hydrolysis not only glucose but also fructose is obtained. Cane sugar is a *di-saccharose* of the composition $\text{C}_{12}\text{H}_{22}\text{O}_{11}$. When it is hydrolyzed it splits and is converted into *two* molecules of mono-saccharoses. One of these molecules is **glucose** and the *other* is **fructose**.



As the glucose is *dextro* rotatory, with a value of $+53^{\circ}$, while levulose is *levo* rotatory, with a value of -92° , it is plain that the mixture of equal

molecules of each must be *levo-rotatory*, with a value of -39° . As we shall find later, cane sugar is also optically active, being *dextro rotatory*, with a specific rotation $(\alpha)_D = +66^\circ$. When, therefore, a molecule of cane sugar is hydrolyzed, with the formation of equal molecules of glucose and fructose, the rotation, which, in the original cane sugar, is *dextro*, is changed to *levo* or, as we say, is *inverted*. The mixture of equal molecules of glucose and fructose which is thus obtained is termed invert sugar and this particular hydrolytic process is called *inversion*. Invert sugar is thus formed whenever cane sugar is hydrolyzed. It is present in honey, which is the chief natural source.

B. DI-SACCHAROSES. $C_{12}H_{22}O_{11}$

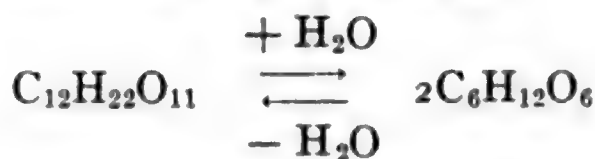
The group of *di-saccharoses*, or poly-saccharoses which are *true sugars*, includes three common and important members. (1) **Cane sugar**, or **sucrose**, perhaps the most important of all the carbohydrates, unless that position may be disputed by starch a poly-saccharose. (2) **Malt sugar**, or **maltose**, found in malt. (3) **Milk sugar**, or **lactose**, the sugar present in milk.

Sucrose, Cane Sugar

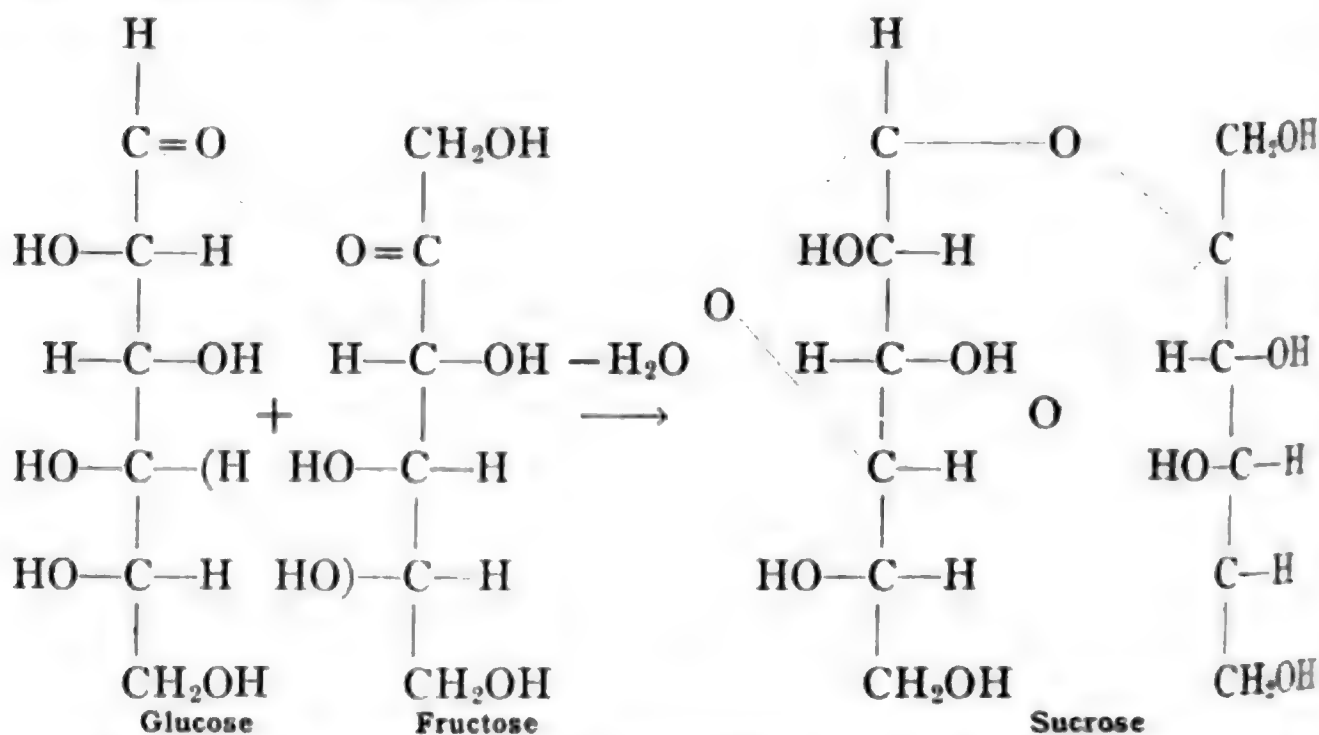
Sucrose, or **cane sugar**, as it is called, because it was formerly obtained almost exclusively from the juice of the sugar cane, is found widely distributed in nature. The chief sources from which it is now obtained industrially, are, (1) *sugar cane*, (2) *sugar beet*, (3) *sorghum cane*, (4) *maple sap*. It occurs in smaller amounts, not sufficient for commercial uses in most plants associated, usually, with glucose or fructose or both. Sucrose is easily soluble in water but only slightly so in dilute alcohol. It separates from water solution in beautiful mono-clinic crystals and is much more easily crystallized than the hexose sugars. It is optically active, being *dextro rotatory*, $(\alpha)_D = +66^\circ$. It does *not form osazones* with phenyl hydrazine, does *not reduce Fehling's solution*, and is *not fermentable* with yeast zymase, nor does it react with hydrogen cyanide. It may be hydrolyzed by means of dilute acids or by means of certain enzymes, viz., **sucrase**, or **invertase**. The products of such hydrolysis are **glucose** and **fructose** as has just been described. It forms salts with some bases, e.g., calcium or strontium hydroxides. These salts are known as *sucrates*.

Constitution of Sucrose.—Both the composition of sucrose, and its

hydrolysis into two molecules of hexose, show that it must be the anhydride of two molecules of hexose sugar.



Also the two molecules of hexose from which sucrose may be considered as being formed are, one an aldo-hexose, and the other a keto-hexose. Its non-activity toward Fehling's solution, phenyl hydrazine, and hydrogen cyanide, indicates that in the sucrose molecule there is *no aldehyde or ketone group*. It will lead us too far to discuss the reasons for assigning the following formula which agrees with the properties of the compound as just given.



Sources and Industrial Processes.—The industrial process of extracting and refining sucrose is most important. The sugar industry is one of the big industries of the world and a brief statement in regard to it will not be out of place. The amount of sucrose present in various plants may be given as follows:

Sugar cane,	15–20 per cent	
Sugar beet,	7–17 per cent	
Sorghum cane,	7–12 per cent	
Maple sap,	2– 3 per cent	<div style="display: inline-block; vertical-align: middle; font-size: 3em; line-height: 1;">{</div> <div style="display: inline-block; vertical-align: middle;"> as much as 12 per cent of this is invert sugar. </div>
Maize stalks,	14 per cent	
Pine apples,	11 per cent	
Strawberries,	5– 6 per cent	

Only the first two of these sources are industrially important so far as obtaining the sugar in a commercial form is concerned.

We shall follow the process as it is carried out with sugar beets though, in general, it is the same, or similar, when the sugar is obtained from the sugar cane. There are three general stages in the process.

1. Extraction of the juice.
2. Concentration of the juice and crystallization of the sugar.
3. Refining of the sugar.

Extraction of Juice.—Originally the cane or beets were macerated by rolling or cutting and then the macerated mass pressed to remove the juice. Where the process is not perfected only about 40–60 per cent of the sugar present in the cane is extracted. Cane juice so obtained usually contains 15–19 per cent sugar and beet juice 20–25 per cent. After the first pressing the extracted mass is moistened with water and a second pressing is sometimes made. By an improved process of extraction by pressure, known as the *Steffen process*, all but about 2.5–5.0 per cent. sugar is obtained from beets.

Diffusion Process.—The most improved process, however, for extracting the sugar from both cane and beets is known as the *diffusion process*. The process depends upon the general property of osmosis. Water, at 70°, to an amount equal to 1.2–1.5 times the weight of the beets, is added to the sliced beets. The action is carried out in a series of compartments and by diffusion and osmosis the sugar is almost completely removed from the beets. Only about 0.3–0.4 per cent sugar remains in the residue. In the case of sugar cane the loss of sugar is reduced to less than 20 per cent of the original amount, *i.e.* to about 3 per cent sugar. The disadvantage of the diffusion process is that the use of so much water increases the cost of the concentration of the juice. The residue left, after the extraction of the juice is known as *bagasse*, and the juice as it is first obtained is termed *raw juice*. The bagasse is used as cattle food or it is dried and used as fuel in some other part of the process.

Concentration.—The next stage in the process is the purification and concentration of the juice and the crystallization of the sugar. The raw juice contains, as impurities, *pectins*, *proteins* and *mineral salts*. These are usually removed by the addition of lime at 85°–90°, which causes the precipitation of the impurities. Care must be exercised however, or some sugar will also be precipitated in the form of calcium

sucrate. As an excess of lime is unavoidable it is necessary, in order to prevent the precipitation of sugar, to pass an excess of carbon dioxide into the solution. This removes the excess of lime and at the same time sets free any sugar combined as sucrate. The liquid is then filtered and the treatment with carbon dioxide repeated a second and third time at 95° and 100° , respectively. The third treatment is sometimes made with sulphur dioxide which decolorizes as well as purifies the solution. This whole treatment with lime and carbon dioxide must be carefully watched or much loss will occur. After the final saturation with gas the purified solution is boiled and filtered when it is ready for concentration.

Evaporation.—The purified juice is clear pale yellow and contains from 10–11 per cent of sugar. The concentration of this juice is usually accomplished by evaporation with steam coils placed directly in the liquid. This evaporation is carried out in pans from which the air has been more or less exhausted, known as *vacuum pans*. They are arranged in multiple batteries so that the steam from the one containing the *more concentrated* juice helps to boil the next one containing *less concentrated* juice. The exhaustion, or vacuum, in the pan containing the *fresh juice*, where it is the *highest*, reaches 640 mm. mercury, and in the pan containing the most concentrated juice the vacuum is about 150 mm. The temperature of boiling in the pans ranges from 56° in the pan with the highest vacuum, *i.e.* the pan containing the *fresh juice*, to 94° in the pan with the lowest vacuum, *i.e.* the pan containing the most concentrated juice.

Crystallization.—After concentration the juice is dark brown in color and contains 50–55 per cent sugar. To bring about crystallization the juice must be filtered and then further evaporated in *simple vacuum pans* until the concentration of the juice is about 85 per cent sugar. The crystallization begins upon the steam coil tubes and when this crystallization reaches a certain point the hot solution, containing considerable crystalline sugar, is discharged from the pan into tanks with stirrers. This crystalline liquid mass is called *massecuite*. This *massecuite* is allowed to cool when it becomes practically a solid mass of crystals wet with liquid. From the crystallization tanks the *massecuite* is passed next to centrifuge machines in which the liquid is thrown off from the crystals. The crystalline sugar thus obtained is a more or less dark colored mass, depending on whether any water or sugar solution

was used for washing in the centrifuge. This first crystalline product is known as *first product sugar* and the liquid thrown off is known as *molasses*. The entire process of evaporation and crystallization is repeated with the molasses. From this second process a *second massecuite*, a *second product sugar* and a *second molasses* are obtained. From this second molasses more sugar may still be obtained by means of a lime or strontia process, but this is not always done. The molasses obtained from beet juice amounts to only about 1.3 per cent and contains about 40–50 per cent sugar. The sugar present in this molasses, though so high in percentage amount, does not crystallize because the molasses contains 8–10 per cent of mineral salts. The presence of these mineral salts prevents the crystallization of five times their weight of sugar. The molasses also contains about 1.5 per cent of invert sugar. The first and second product sugars are now ready for refining.

Refining.—The combined first and second product sugars are called *raw sugar*, and contain 88–96 per cent sugar. The refining of this raw sugar consists, essentially, in re-solution, purification and decoloration, evaporation and crystallization. The purification is usually accomplished by decolorizing with animal charcoal and filtering. Sodium thio-sulphate is sometimes used as a decolorizer. To destroy the last traces of yellow color, a very small amount of ultra-marine blue was formerly added. As a result of all these treatments the crystalline sugar finally obtained is pure white granulated sugar.

History and Statistics.—A few facts of history and statistics may be of interest. The first sugar material used was, probably, honey, containing, as previously stated, invert sugar. The sugar cane has been known since ancient times in China, India, Egypt, Greece, etc. Sugar was a commercial substance in the seventh century. The culture of the sugar cane was introduced into Brazil and the West Indies in the fifteenth century. At the present time it is grown in Cuba, Philippine Islands, Jamaica, Louisiana, Brazil, Peru, China, Japan, India, Egypt and Australia. The extraction of sugar from beets was first accomplished commercially at the very beginning of the nineteenth century, but only about 3 per cent of the sugar was obtained. Except for a short time, viz., from 1806–1814, when Europe was closed to the importation of cane sugar, it was not successfully prepared until about 1828 in France and 1836 in Germany. In 1865 *one and one-half million tons* were produced. In 1866 beet sugar was only 30 per cent of

a total sugar production of *three million tons*. In 1887 it was 47 *per cent* of *five million tons*. In 1899 it was 64 *per cent* of *seven and one-half million tons*. In 1901 it was 67 *per cent* of *nine million tons*. In 1910 it was 46.5 *per cent* of *fifteen million tons*. In the United States sugar cane is grown, chiefly, in Louisiana, and the Philippine Islands. The sugar beet, chiefly, in Michigan, Wisconsin, Colorado, Kansas and Nebraska. In the United States there has usually been a tax upon the importation of refined sugar but no tax upon the importation of raw sugar, containing less than a certain *per cent* of pure sugar. Thus, in this country sugar is imported as raw sugar and refined after importation. On account of the above statement in regard to the tax upon sugar, it is necessary to determine accurately, the amount of pure sugar in raw sugar.

Analysis.—The analysis of sugar is carried on, almost entirely, by the use of the polariscope. As sucrose has a definite optical rotation the determination of the rotation of a sugar solution gives us a means of accurately determining the amount of pure sucrose in any sugar solution or sugar material.

Polariscopes used for this particular purpose are called *saccharimeters*, and the scale indicating the angle of rotation is graduated so as to read, *per cent sugar* instead of *degrees rotation*. In the ordinary analysis of plants and food materials which contain more or less sucrose the sugar is usually determined by the precipitation method with *Fehling's solution*, after first hydrolyzing the sucrose to **invert sugar**. This method gives us, of course, the amount of invert sugar but this may readily be calculated back to the equivalent amount of sucrose. The sucrose content of solutions which are free from other substances may also be calculated from the specific gravity. The ordinary forms of immersion spindle hydrometer specially graduated to read *per cent sugar* are known as *saccharometers*. The special form most commonly used in sugar work is known as a *Brix* hydrometer or *saccharometer*, and the term *degrees Brix* means *per cent sugar*.

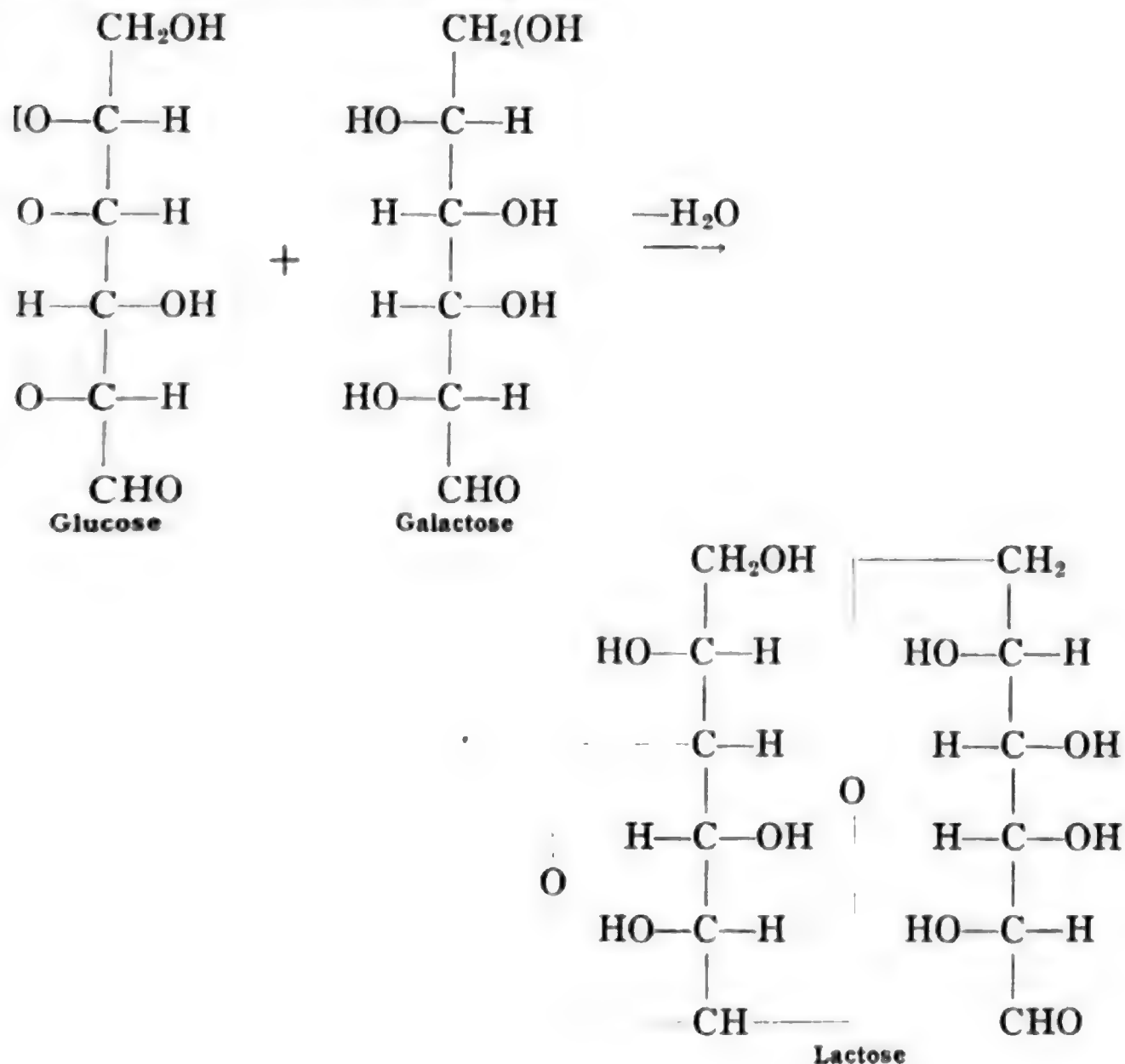
Lactose, Milk Sugar

The second important di-saccharose is the sugar which is present in milk and on that account is known as **lactose** and also as **milk sugar**. The amount of lactose present in milk is about 3–6 *per cent*. It crystallizes in large white crystals containing one molecule of water which it loses at 130°. The anhydrous sugar melts at about 200°.

soluble in water and is optically active, being dextro rotatory, $(\alpha)_D = +52.5^\circ$. It is not fermented by yeast zymase and it yields an osazone of very fine needle crystals. Lactose differs from sucrose in an important point, viz., it *reduces Fehling's solution*. It must, therefore, have the constitution of either an aldehyde or ketone compound. On hydrolysis it splits and yields two molecules of hexose sugar, one of the molecules being **glucose** and the other **galactose**. As galactose, according to the formulas given on page 344, is also an aldo-hexose, like glucose the formula for lactose, being the anhydride of these two hexose molecules, would probably contain an aldehyde and not a ketone group. Also as all three of these sugars are dextro rotatory there is *no inversion when lactose is hydrolyzed*.



The full constitutional formula for lactose is similar to that of sucrose but contains one aldehyde group.



Maltose, Malt Sugar

Malt.—The third important di-saccharose is **maltose**, or **malt sugar**, which, as its name indicates, is found **in malt**. Malt is the sprouted grain of barley or any other cereal. Usually the name malt applies to that obtained from barley. When these grains sprout an enzyme known as **diastase**, converts the starch of the grain into maltose. The action is one of hydrolysis and will be discussed again under starch. The malted grain is extracted with water and the maltose which is held in solution in the water is obtained by the evaporation of the water and the crystallization of the sugar. Maltose is also obtained as a thick syrup. The sugar is easily soluble in water and crystallizes in fine white needles containing one molecule of water, which is lost at 100° . It is optically active, being *dextro* rotatory like glucose, lactose and sucrose. Its specific rotation is considerably higher than the other sugars, $(\alpha)_D = +137^{\circ}$. When maltose is hydrolyzed by the action of acids or the enzyme, **maltase**, it splits into two molecules of hexose sugar, exactly as the other two disaccharoses, but the product of the hydrolysis is **glucose alone**, *i.e.*, one molecule of maltose yields *two molecules of glucose*. In this hydrolysis there is *no inversion*.



Maltose *reduces Fehling's solution* and therefore probably contains an aldehyde group. The constitutional formula is probably the same as that given for lactose. It yields an osazone which crystallizes in tufts of needles which are more blunt than the crystals of glucosazone. Maltose, like the other di-saccharoses does *not ferment with yeast zymase*.

Alcoholic Fermentation.—The statements, just made, in regard to the alcoholic fermentation of the di-saccharoses, need to be explained. Yeast, *i.e.*, ordinary beer yeast, contains several enzymes. The definite enzyme present in yeast, and which, alone, produces alcoholic fermentation of sugars, is the enzyme **zymase**. This enzyme acts *only upon* the hexoses **glucose, fructose, and galactose**. It has no action upon either of the three di-saccharoses we have mentioned. When, however, cane sugar or malt sugar is treated with ordinary yeast alcoholic fermentation takes place. This is due to a preliminary action of *other* enzymes upon the di-saccharoses by means of which they are converted into mono-saccharoses and then the mono-saccharoses are fermented.

by the yeast zymase. The particular enzyme which hydrolyzes **sucrose** is known as **sucrase**, while the one hydrolyzing **maltose** is, **maltase**. Both of these di-saccharose hydrolyzing enzymes are found in yeast so that yeast, containing a mixture of several enzymes, will ferment the two di-saccharoses sucrose and maltose. Lactose is wholly unaffected by yeast because the lactose hydrolyzing enzyme, **lactase**, is *not* present in yeast. All three of these di-saccharoses are hydrolyzed in the digestive tract of animals.

C. TRI-SACCHAROSES. $C_{18}H_{32}O_{16}$.

Raffinose

Only one tri-saccharose is important. It is known as **raffinose** and has the composition $C_{18}H_{32}O_{16}$. It is found in beets and is present in the molasses after the sucrose sugar is crystallized out. It is also found in barley and in cotton seeds. When this tri-saccharose hydrolyzes it yields first a di-saccharose known as **melibiose** and a mono-saccharose **fructose**. The di-saccharose is then further hydrolyzed and yields two molecules of mono-saccharose, viz., **glucose** and **galactose**. The complete hydrolysis of the tri-saccharose, therefore, is as follows,



D. POLY-SACCHAROSES. (not sugars). $(C_6H_{10}O_5)_x$.

The poly-saccharoses which are not true sugars, are usually called simply, *poly-saccharoses*. The most common and important ones are the following,

Starch, widely distributed in plants as reserve food, not found in animals.

Cellulose, widely distributed in plants as the fibrous or cell wall substance.

Glycogen, present in the liver and muscles of animals; also known as animal starch.

Dextrin, an intermediate hydrolytic product between starch and maltose; sometimes present in plants.

Inulin, similar to starch and found in certain plants, especially in the tubers of the Dahlia.

General Character.—The poly-saccharoses are compounds made up of an unknown number of hexose mono-saccharose units. The com-

position is represented by the formula, $C_6H_{10}O_5$, but as the molecular mass is unknown, it is written, $(C_6H_{10}O_5)_x$. On hydrolysis by means of acids or enzymes, the poly-saccharoses all yield finally hexose mono-saccharoses, as follows,

Starch	→	Glucose
Cellulose	→	Mannose, Galactose, Glucose.
Glycogen	→	Glucose
Dextrin	→	Glucose
Inulin	→	Fructose

In the case of starch, dextrin and probably glycogen, the di-saccharose, maltose is an intermediate product of the hydrolysis. When hydrolyzed by enzymes two or more distinct enzymes are necessary to complete the hydrolysis of the poly-saccharoses to mono-saccharoses. With acids the hydrolysis goes through to the final product though the intermediate products are probably formed.

Solubility.—The poly-saccharoses differ from the sugars in the absence of a sweet taste, in their non-crystalline character and in their general insolubility. Inulin and dextrin are soluble in water, glycogen is soluble to an opalescent liquid, while starch and cellulose are insoluble. In hot water starch forms a colloidal solution or emulsion known as *starch paste*. Starch reacts with a solution of iodine and gives a beautiful *blue* color. This is a characteristic reaction for starch and is used as a qualitative test, especially in microscopic examination. Dextrin exists in several forms, one of which known as **erythro-dextrin** gives a *red* color with iodine.

Iodine Reaction.—The other forms of dextrin known as **achroo-dextrins**, give *no color with iodine*. The following enzymes act upon the different poly-saccharoses hydrolyzing them as indicated:

Enzymatic Action.

Starch	+ Diastase	→	Dextrins	→	Maltose.
Dextrin	+ Diastase	→	Maltose		
Cellulose	+ Cellulase	→	Mannose + Galactose		
	(Cytase)				
Glycogen	+ Glycogenase	→	Glucose		
Inulin	+ Inulase	→	Fructose		

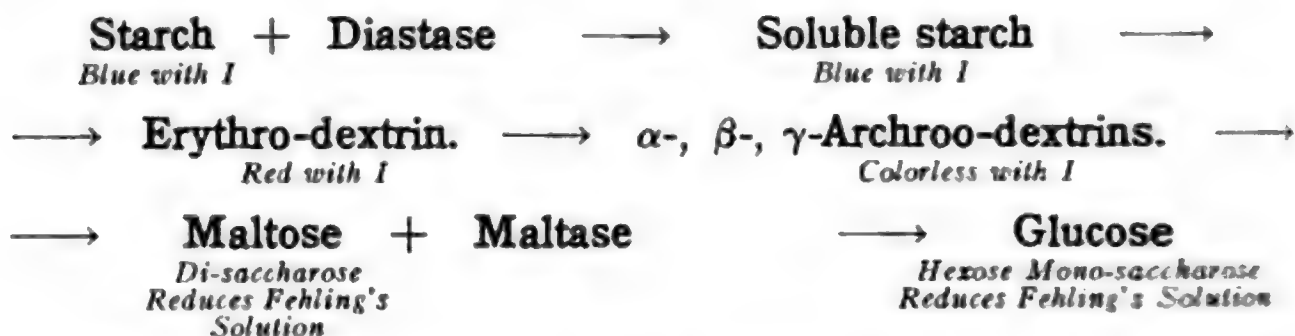
We may now consider a few facts and additional properties of individual poly-saccharoses.

Starch

Photo-Synthesis.—With the exception of sucrose, starch is probably the most important of the carbohydrates, considered as a food or in its other commercial uses. It is found in practically all green plants and is a reserve food material. It, therefore, occurs most abundantly in *seeds, roots, tubers, etc.* It is synthesized, by the photo-synthetic process in the leaves, from the **carbon dioxide** in the air and **water** obtained mostly from the soil. The *energy* for this synthesis is derived from the *sun*, so that only in sun-light is the synthesis effected. Hence the process is termed *photo-synthesis*. The active substance in the leaves which effects the synthesis is **chlorophyll**, or green coloring matter. Thus only in green plants is this photo-synthesis brought about. The intermediate products of the synthetic process have not been established. It seems probable that **form-aldehyde** is the first compound formed, which, by condensation, or polymerization, is converted into a carbohydrate, probably **glycerose**, which again may be polymerized into **fructose** (α -**acrose**) and **glucose**. These steps have been discussed in connection with the consideration of the triose, glycerose and also in connection with the hexose sugars, glucose and fructose. From glucose starch could be formed by condensation with the loss of water. Whether sucrose is formed as an intermediate product is not proven. The final product, of photo-synthesis, however, is **starch**. After thus being synthesized in the leaves, the starch is hydrolyzed by the enzyme, **diastase**, present in the leaves, to maltose, which is also hydrolyzed by **maltase**, likewise present, and the final product of these hydrolyses is **glucose**.

The glucose, thus formed, being soluble, is transported through the plant by means of the plant sap and is used in the cells as *energy food*. The excess of glucose, not used as food, is again converted into the form of starch and is deposited in the form of *starch grains* as a *reserve food material* in the reserve organs of the plant, viz., *seeds, roots, tubers, etc.* When the seed germinates, as in germinating barley, or malt, the same enzymes, diastase and maltase, which are present in the seed, again hydrolyze the starch into glucose. This now becomes the food material for the growing plantlet, up to the time when, by the development of the aerial green parts of the plant, it becomes able to synthesize its own food material from the carbon dioxide and water of the air and soil. In this hydrolysis of starch, especially in the seeds, several intermediate

products have been isolated or proven to exist. The entire action may be represented as follows,



By the action of acids the same hydrolysis is effected, though all of the intermediate products have not been isolated or proven.

These hydrolyses indicate that starch is a compound existing as a complex molecule containing numerous mono-saccharose groups united in an *anhydride constitution*, similar to that shown to exist in the case of the di-saccharoses. The molecular mass of starch is unknown, but has been claimed to be that represented by the formula,



Starch is present in plants in distinct granular form. The starch grains from different plants possess characteristic structures, shown by microscopic examination, *e.g.*, *potato starch*, *wheat starch*, *arrow-root starch*, etc. These starch grains are wholly insoluble in water. When boiled in water the starch grain pellicles break and the starch is set free in such a form that it produces a colloidal solution with water. This colloidal solution is opalescent and is known as *starch paste*. Both in the granular form and in the starch paste the starch gives the *blue* color reaction with iodine solution. Starch paste is best prepared as follows. Grind up about one gram of starch with just sufficient cold water to form a thin mixture. Boil about 1000 c.c. of water and while boiling add the starch mixture and continue to boil until a mucilaginous paste is formed. Starch paste, so made, should not separate on standing. Starch contains, usually, about 10–20 per cent. of water, which may be completely driven off at 110° .

Industrial Uses.—The industrial applications of starch are;

1. The most important use of all is as a *food stuff*. As starch occurs naturally in most plants, it is the most abundant of all carbohydrate food materials for animals and human beings. As a food, starch is used mostly in its naturally occurring form in the plant, such as

potatoes, various roots, *e.g.*, carrots, beets, parsnips, etc.; in grains, *e.g.*, wheat, oats, rice, corn, etc.; and in greater or less quantity, in almost all plants or plant parts that are used as food.

2. *A source of alcohol* and alcoholic beverages. The starch of grains, potatoes, etc., is first hydrolyzed by natural sprouting, as in the preparation of barley malt, or by the addition of malt to it. The hydrolytic products, glucose and maltose, are then fermented by the addition of yeast, containing the enzymes, **maltase**, and **zymase**, and alcohol is thus produced. This has been fully discussed in the chapter on alcoholic fermentation, (p. 95).

3. *A source of commercial glucose*. Starch from various sources, *e.g.*, corn, potatoes, etc., is hydrolyzed by boiling with dilute sulphuric acid, by which the final hydrolytic product, glucose, is obtained. It is ordinarily obtained as a thick syrup, *corn syrup*, or as a crystalline substance, **glucose**. Corn syrup as usually made is not pure glucose syrup but contains more or less of the intermediate products, dextrin and maltose. With these present the syrup does not crystallize even when very concentrated.

4. *As a coating or sizing* for paper, cloth, etc., in the form of the mucilaginous starch paste. Also as an adhesive.

Isolation of Starch.—Starch is also used as a food in its pure form. To obtain this the plant part, *e.g.*, potatoes, corn, etc., is macerated and then stirred up with a large amount of water. The watery mass is passed through sieves to remove the fibrous material while the starch, in suspension, passes through. On allowing the starchy liquid to settle the starch is obtained as a sediment in quite pure condition. As the materials used contain relatively little else than starch and water there is not much foreign substance present. Starch so prepared is the common form in which it is sold under the names of *corn starch*, and *laundry starch*, the former used as a food and the latter as a laundry sizing material.

The three most common substances used as a source of pure starch contain the following amounts.

Plant material	Calculated on fresh substance, per cent.	Calculated on dry substance, per cent.
Potatoes, (tubers)	18-21	72-84
Wheat, (grain)	56-65	66-72
Corn, (grain)	62-65	68-72

Cellulose

Another poly-saccharose which rivals starch in its wide distribution in nature and in its economic importance is **cellulose**. It occurs as a universal constituent of the cell wall of plants. In young cells it is probably pure but in older cells, especially in the woody tissue of large plants such as trees, it has become hardened by the infusion of gums and resins. Several special forms of cellulose occur as the fibres of various plants such as *cotton*, *flax* (linen), *hemp*, *sisal*, a variety of *hemp*, *jute* and *wood*. The fibres of these plants have great industrial uses and give to cellulose an immense economic value. Cotton fibre is practically pure cellulose. The name cellulose applies not to a single individual compound but rather to a group of compounds of similar character and occurrence. While it is practically found only in plants it is known to occur in some animals. **Tunicin** is an example of an animal cellulose found in *tunicates* and is considered identical with vegetable cellulose.

Normal Cellulose.—Several varieties or forms of cellulose are known as found in plants. Cotton fibre is a typical and practically pure cellulose. This form which occurs also in flax and hemp is termed **normal cellulose**. On hydrolysis it yields **glucose** sugar as the final product. In speaking later of the chemical properties of cellulose it is the normal cellulose which is considered. Cotton fibre contains about 89-91 per cent. pure cellulose, 8-10 per cent. water and only about 1 per cent. of other compounds including salts, fats and proteins. Flax and hemp stalks yield about 72 per cent. cellulose.

Hemi-Cellulose.—**Hemi-cellulose** is the name applied to a form of compound which is found in numerous seeds such as peas, beans, coffee, etc., and which differs in form from the fibrous variety. It is probably simpler or perhaps purer than normal cellulose and hydrolyzes more easily. On hydrolyzing celluloses of this type yield the hexose mono-saccharoses, **mannose** and **galactose** and also **pentose** mono-saccharoses. They are therefore included in the group of poly-saccharoses termed **mannans**, **galactans** and **pentosans** (p. 380). The reserve food cellulose of germinating seeds belongs to this type.

Compound Celluloses.—Differing from both of the preceding varieties are the celluloses which are present in the *cork tissue* and *wood* of trees, in the *stalks of jute* and *ripe grasses*, especially the *cereals*, and in the *parenchymatous tissue of fruits*. The celluloses of this type are

termed **compound celluloses** because they consist of two parts, viz., a cellulose part and a non-cellulose part. The two parts are probably in real combination. The compound celluloses are of three classes.

Ligno-Cellulose.—As the pure cellulose of young growing cells becomes older, in the ripening of grasses or in the formation of the woody tissue of trees, the cellulose becomes changed by the infusion of, and probable combination with, gums and resins that are termed in general **lignins**. These lignins are probably of pentosan character. The resulting compound cellulose is termed **ligno-cellulose**. Wood from spruce trees yields about 50–55 per cent. of pure lignin-free cellulose while hard woods like oak yield only about 35 per cent., and jute stalks yield about 54 per cent.

Pecto-Cellulose.—In the parenchymatous tissue of grasses and of fruits the original pure cellulose is changed to a compound cellulose by combination with gummy compounds known in general as **pectins**, the compound cellulose being termed a **pecto-cellulose**. The pectins also are probably of pentosan character. When these pecto-celluloses are hydrolyzed by boiling the pectin compounds are set free and on cooling gelatinize. The formation of fruit jellies is the result of such a change.

Adipo-Celluloses.—The third type of compound cellulose has a non-cellulose constituent of a *fatty* character known as **cutin**. The compound cellulose is therefore termed an **adipo-cellulose**, or a **cuto-cellulose**. Cellulose of this variety is formed in the *cork tissue* of plants and trees.

In all of these occurrences the compound celluloses are usually associated with more or less normal cellulose.

Properties of Cellulose.—In its physical character cellulose possesses different properties such as fibrous, cellular or woody as has just been discussed. It is non-crystalline and probably colloidal.

Schweitzer's Reagent.—Chemically it is an inert compound wholly insoluble in water, most neutral reagents and in dilute acids or alkalies under ordinary conditions. It is probable that no solvent dissolves cellulose without decomposition or hydration. The solvent most commonly used is an ammoniacal solution of copper oxide made by dissolving freshly precipitated copper hydroxide in ammonium hydroxide. This solution is known as **Schweitzer's reagent**. After solution in this reagent acids reprecipitate the cellulose as a hydrated cellulose.

Similarly a concentrated solution of zinc chloride dissolves cellulose as a hydrated product.

Xanthic Acid.—Another solvent of cellulose is **xanthic acid**, also called xanthonic or xanthogenic acid. Xanthic acid is the **ethyl ether of di-thio-carbonic acid**. Its formula is $\text{HS-CS-OC}_2\text{H}_5$. When heated with water to 500° under pressure cellulose is dissolved and undergoes decomposition.

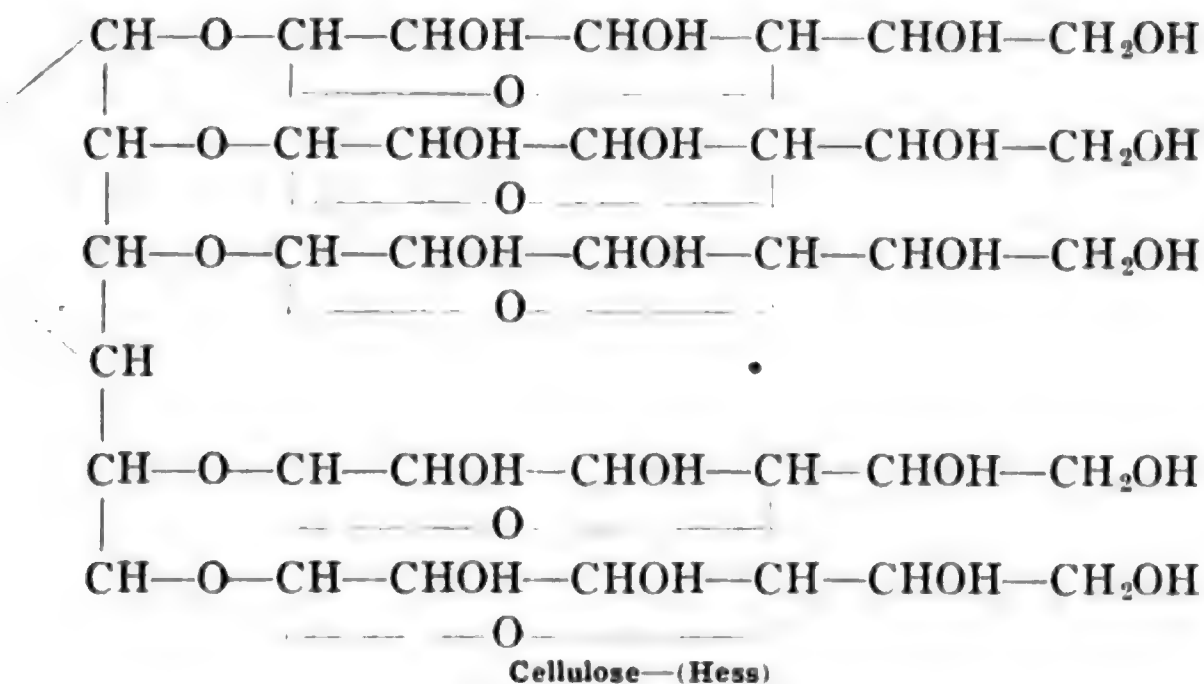
Amyloid.—When treated with concentrated sulphuric acid cellulose dissolves and undergoes hydrolysis. If the solution is diluted with water a gelatinous product is obtained which gives the blue color with iodine characteristic of starch. This product is known as **amyloid**. When boiled in the dilute acid the amyloid is hydrolyzed and dextrin and finally glucose are obtained. Concentrated **hydrofluoric acid** and **phosphoric acid** also dissolve cellulose. With glacial acetic acid in the presence of acetic anhydride and sulphuric acid cellulose yields acetyl derivatives indicating its alcoholic character. From the products of this reaction the acetate of a di-saccharose is obtained.

Cellobiose.—This di-saccharose is known as **cellobiose**. With dilute nitric acid, sp. gr. 1.25, cellulose is converted into oxy-cellulose.

Nitro-Cellulose.—Concentrated nitric acid together with sulphuric acid however yields *nitric acid esters* of cellulose known as **nitro celluloses** which have important industrial uses as will be discussed presently. By complete oxidation of cellulose with nitric acid **oxalic acid** is obtained. Dilute solutions of alkalies below about 10 per cent. have no action on cellulose. When however cellulose is treated with a solution of sodium hydroxide above 10 per cent., best from 18 per cent. to 28 per cent. sodium cellulose is formed and this with water yields a hydrated cellulose. By this treatment the fibrous character of cotton remains but the fibres possess entirely new properties. This is the basis of what is known as **Mercerized cotton** (p. 372). On prolonged treatment with strong alkalies or by fusion cellulose is oxidized to oxalic acid

Constitution.—A study of the hydrolytic products obtained from cellulose indicates that it is a polysaccharose carbohydrate made up of *hexose mono-saccharose units* and in the hemi-celluloses and probably the ligno-celluloses the units may also be *pentose mono-saccharoses*. Normal cellulose is probably composed of *glucose units only* while the hemi-cellulose may contain *mannose or galactose units*. In regard to

the size of the molecule all the evidence indicates that it is larger and probably more complex than starch as shown by the formation of amyloid. That it is not simply a larger molecule than starch is indicated by the fact that from the two compounds different di-saccharoses are obtained, starch yielding maltose whereas cellulose yields cellobiose. In any poly-saccharose made up of a large number of hexose units by the loss of water from each two units linked together as illustrated in the constitutional formulas for the di-saccharoses (p. 354) it will be seen that there will be possible *only three hydroxyl groups* in each C_6 unit. This is important in connection with the formation of nitric acid esters and is supported by the fact that complete nitration of cellulose results in the *tri-nitric acid ester* if six carbon atoms are considered as the unit. A formula, consisting of six hexose units, has been suggested by Hess.



Industrial Uses of Cellulose

Cellulose is a substance of immense economic value because of the industrial uses made of it. As a food stuff it is of importance only in connection with herbivorous animals. The products made from it are numerous but may be considered under two heads. I. *The utilization of the fibrous forms of cellulose*, more or less purified but unchanged chemically, for the manufacture of *fabrics* or other materials in which the fibre is the important thing. This includes all kinds of *cotton, linen, hemp and jute* goods in the form of *thread, string, rope or cloth* and also *paper* of all kinds. II. *The transformation of cellulose by chemical change* into products which

may retain the fibrous character but which in most cases are wholly different from the original material. This includes the manufacture of such products as **Mercerized cotton, artificial silk, celluloid, collodion and cellulose explosives** such as **gun cotton**.

Cotton and Linen Cloth, etc.—The two most important sources of cellulose for the manufacture of thread and cloth and similar articles are the *boll* of the *cotton plant* and the *stalk* of the *flax plant*. The former is the source of all goods known as *cotton* while the materials made from the latter are termed *linen*. Another important fibre plant is *hemp*, the leaves or stalk of which yields fibres which are principally used in making *twine, rope* and *canvas*. Several varieties of hemp are used such as *manila hemp, sisal*, etc. The *stalk* of the *jute plant* is the source of materials out of which *sacking* or *burlap* and *carpets* are made. In the manufacture of these products the fibre of the plant is mechanically separated and then spun into thread or twisted into yarn or rope. The thread or yarn are then woven into fabrics. The products possess properties characteristic of the particular fibre used. As in the manufacture of all of these important materials the cellulose undergoes no chemical change but is simply mechanically treated no further details of the processes will be given.

Paper.—In the manufacture of **paper** the cellulose also undergoes no chemical change other than purification and, in the case of ligno-cellulose of wood, conversion largely into normal cellulose. Pure unsized paper, such as the so-called *ashless filter papers* for analytical purposes, is practically pure cellulose. The raw materials for the manufacture of paper are *cotton* and *linen rags, wood, straw and hemp*. The best grades of writing paper, *bond papers*, were originally made wholly from linen fiber but now other materials are used together with linen. The common paper such as that used for newspapers is made wholly or largely from wood. The woods used are *fir, pine, larch, poplar, birch and beech*.

Wood Pulp.—The methods for converting the wood into pulp are two, viz., *mechanical* and *chemical*. In the former the wood is mechanically cut into pieces, the knots removed and then the pieces shredded into fibrous material and carried away by water. By the action of water it is converted into a pulp and separated into grades by means of sieves. The fine watery pulp is then pressed into sheets and dried. The product is known as dry pulp and is stock material for making

over into finer grades of paper. In the *chemical process* the wood is similarly cut into pieces and freed from knots. The small chips of wood are then disintegrated and converted into pulp by the chemical action of either **sodium hydroxide** under pressure and at a temperature of 170° or more commonly by the action of **acid sulphites** of **calcium** or **magnesium**, $\text{Ca}(\text{HSO}_3)_2$ and $\text{Mg}(\text{HSO}_3)_2$. These acid sulphites are made by the action of **sulphur dioxide** and **water** upon calcium or magnesium *lime stone*. The acid sulphite liquor is introduced into large digesters filled with the wood chips and heated under pressure to 130° . After digestion the soft pulp is removed, washed with water and carried away by water through a series of sluice ways and sieves. By this means the pulp is separated into grades and the fine pulp carried finally to large bleaching vats where it is bleached by the action of **chlorine** usually. The bleached pulp is then carried by water over fine wire gauze where it drains of much water and then it is passed to heated rolls from which it emerges as dry sheet pulp. The yield of dry pulp by either process is about 50–55 per cent. of the wood used. An electrical process has also been used in which sodium chloride is decomposed by the electric current, the wood being present during the electrolysis. The result of the electrolysis is to produce **chlorine**, **hypochlorous acid** and **sodium hydroxide**, all of which effect the disintegration of the wood.

The conversion of the dry pulp or other paper stock into finished paper is accomplished in general as follows. Most paper is a mixed product of several stock materials such as wood pulp and pulp from cotton and linen rags. The dry wood pulp together with varying proportions of cotton rags and linen rags are mixed with water and thoroughly disintegrated. This is accomplished in large drum-like vats with stirrers and sieves known as *hollanders*. After thorough stirring a homogeneous mixed pulp is obtained ready for the rolls. During the mixing further bleaching is usually effected and blueing may be added to neutralize traces of yellow color. Also inert substances such as **barium sulphate** or **zinc oxide** are added to give weight and **rosin** is used for *sizing*. The pulp is then drained over copper gauze and passed to the rolls. Before passing onto the rolls the paper may be passed through a sizing bath to give a smooth gloss surface. From the rolls, some of which are heated, the paper is taken off as finished product. The different grades and qualities of paper depend upon both the character

of the original raw material used and upon the degree of purification to which it has been subjected.

Production and Consumption.—A few statistics of the production and consumption of paper may be of interest. In 1906 the world's production of paper amounted to about eight million tons. In 1904 the United States produced two million tons of pulp and four million tons of paper. The amount of paper used annually per inhabitant is about as follows:

United States	41.8 lbs.
England	37.4 lbs.
Germany	30.8 lbs.
France	25.3 lbs.
China	1.3 lbs.

Parchment Paper.—We have previously spoken of the solvent action of concentrated sulphuric acid on cellulose. If instead of letting the action of the acid continue until disintegration of the cellulose occurs it is stopped soon after it begins and the acid removed by thorough washing with water the paper is converted into a hard, tough and semi-transparent product which is known as **parchment paper**.

Mercerized Cotton.—Within recent years, since about 1896, a form of cotton known as **Mercerized cotton** has become a definite article of commerce. It is made from cotton, usually in the form of thread or cloth, by chemical treatment. As early as 1844 **Mercer**, from whom the material is named, found that cold sodium hydroxide solution of about 20°–30° Baumé, (14–24 per cent.) converted cotton cloth into a stronger more silky material which can be dyed more easily than the untreated cotton. The chemical and physical changes taking place have been shown to be as follows: The cold alkali converts the cellulose into a sodium cellulose compound, and this on washing with water is converted into a *hydro-cellulose*. The general fibrous form remains unchanged but the fibers which are originally flat become cylindrical and thicker or more compact increasing in weight by 8–10 per cent. It is also smooth and translucent in character and possesses a luster similar to that of silk. On drying the fiber shrinks to 75–80 per cent. of its original length and increases in strength by as much as 68 per cent. If the process is carried out while the material is held under tension the shrinking is prevented while the thickening and change in

luster take place as originally stated. The increase in strength under tension is usually about 35 per cent. The silky character of the product may be increased by treatment with calcium acetate, soap and acetic acid successively. Not only, however, does Mercerized cotton look and feel like silk but its action toward dyes is also like that of silk and it can be colored by many dyes impossible of use on cotton. On account of these desirable properties it has become an important article of trade.

Artificial Silk.—While Mercerized cotton has the general appearance of silk it is not what is known as **artificial silk** which, while also a cellulose product, is the result of more thorough chemical reaction. Artificial silk is made by several processes and the different varieties differ slightly though the chemical nature of the products is probably much the same. The raw material in all processes is cellulose, usually in the form of cotton waste or wood fiber.

I. From Mercerized Cotton.—When the sodium cellulose produced in Mercerizing cotton is dissolved in ammoniacal copper oxide (Schweitzer's reagent) and the solution poured into sulphuric acid the cellulose is reprecipitated as an *oxidized hydro-cellulose*. In practice the cotton waste after purification is treated with sodium hydroxide, copper sulphate and ammonium hydroxide and allowed to digest until it has dissolved to a stringy mass. This is then filtered under pressure and the cellulose solution is forced through a fine set of capillary tubes into a coagulating solution. This coagulating solution may be sulphuric acid or better a 5 per cent. solution of sodium hydroxide which is followed by a dilute sulphuric acid bath to remove copper hydrate. The resulting coagulated cellulose is in fine filaments which are spun into thread and then woven into other desired forms.

II. From Nitro Cellulose.—Historically the first artificial silk was made from nitro cellulose by **Chardounet** in 1885. **Collodion** is a mixture of the lower **nitro celluloses** or *nitric acid esters of cellulose* made by nitrating cellulose incompletely. It had been found that fine fibers of collodion could be used in preparing the carbon filaments for incandescent electric lights. This led **Chardounet** to try spinning the filaments of collodion, which he did and obtained a product termed artificial silk. The collodion solution in alcohol-ether is forced through fine capillaries as in the preceding process and as the solvent rapidly evaporates, fine fibers of artificial silk are obtained which may be con-

verted into thread and other materials. The artificial silk so made is still nitro cellulose and while not explosive it is very inflammable. To make it safe to use, the nitro cellulose is denitrated by means of **ferrous chloride**, **formaldehyde** or better by means of **ammonium hydrogen sulphide**. The denitrated product is probably a *hydro-cellulose* of similar character to that obtained from Mercerized cotton and it possesses the same silk-like character.

Viscose Silk.—III. **From Cellulose Xanthate.** We have referred to the solvent action of **xanthic acid**, which is the **ethyl ether of di-thio-carbonic acid**, viz., $\text{HS-CS-OC}_2\text{H}_5$. When sodium cellulose is dissolved in xanthic acid the cellulose is in the form of **sodium cellulose xanthate**. A solution properly prepared by treating cellulose with **sodium hydroxide** and **carbon di-sulphide** in the presence of **benzene** or **carbon tetra-chloride**, in which polymerization of the cellulose compound is effected, is decomposed by forcing capillary streams of the solution into a solution of **ammonium sulphate**. The cellulose is thus obtained as in the other processes in the form of fine filaments of a **hydrated cellulose** possessing silk-like properties. Artificial silk of this type is known as **viscose silk** and is made in large quantities. In 1914 about 20,000,000 pounds of artificial silk were made, of which about 3,000,000 pounds were made in the United States. Most of this product was **viscose silk**.

IV. **From Cellulose Acetate.**—Solutions of **cellulose acetate** are prepared by treating cellulose with a mixture of **acetic** and **phosphoric acids** and dissolving the product in **chloroform** or better in **formic acid** or in **tetra-chlor ethane**. The solution of cellulose acetate is treated and converted into filaments and then into thread and other materials by similar methods to those already given.

In all of the varieties of artificial silk which we have mentioned the product is probably in the form of *hydrates* or *oxidized hydrates* of cellulose. This cellulose compound is obtained as fine filaments by spraying the solution of the cellulose, in one of the various solvents, into a coagulating solution. The filaments are then spun into thread and converted into other forms desired. Whether as fiber, thread cloth or other material the product possesses silk-like properties both as to luster, feel and ability to react with dyes. It thus has many advantages over ordinary cotton. All of the varieties of artificial silk are, however, inferior to silk itself in strength, especially when wet.

and in fineness of the fiber. In luster they even surpass silk. An illustration of the difference in fineness of fiber is the fact that the filaments of the silk cocoon require *six to seven million meters* to weigh one kilogram whereas the finest fibers of viscose silk require only *one million meters* for the same weight.

Nitric Acid Esters.—As cellulose is a *poly-hydroxy alcohol* in constitution it forms *esters* with acids. The acetate and nitrate esters have both been referred to in connection with artificial silk. The esters of cellulose and nitric acid, usually termed **nitro celluloses**, have other exceedingly important uses. The higher nitrates are *direct explosives* such as **gun cotton** and the lower nitrates are the basis of many *mixed explosives* and *smokeless powders* and also of the very important substance known as **celluloid**. In discussing the constitution of cellulose we referred to the probability that in such a compound, which is an anhydride of hexose mono-saccharose units, there will remain in each unit of six carbon atoms only *three* hydroxyl groups with which the compound may react with acids forming esters. This is borne out by the fact that the highest nitric acid ester obtained contains only *three* nitric acid groups per unit of six carbon atoms. It is claimed that higher esters have been prepared but it is probable that in them more than six carbon atoms are considered in proportion to the nitric acid groups. The exact constitution or even composition of the cellulose nitrates used in the important products mentioned is unknown due to the character of the reaction of nitration. The reaction is progressive and more and more nitric acid enters the cellulose molecule as the reaction continues by indefinite stages. The result is a series of nitrates which are mixed in some instances with hydro-celluloses, oxy-celluloses and nitrates formed from them and also with other esters formed with the sulphuric acid always present during nitration. It is thus not surprising that no nitrate of cellulose or derivative of it has ever been prepared as a distinct individual. Neither has one ever been crystallized, distilled or vaporized unchanged. We thus see that statements in regard to the composition of the various products made from these esters must be more or less general and indefinite. Furthermore, the nomenclature of the products is somewhat confused due to the variety of uses to which they are put.

Pyroxylin.—The term **pyroxylin** is generally used in this country as applying to the lower cellulose nitrates containing about 10.5–12.2

per cent. nitrogen, which are soluble in amyl acetate and in methyl alcohol and are used in preparing *lacquers* and in making *artificial silk* and *celluloid*.

Collodion.—**Collodion** and **photo-cotton** are terms often used practically synonymously with **pyroxylin** but apply more specifically to lower nitrates, soluble in alcohol-ether. Collodion is used in pharmacy and as a coating for sensitive photographic plates.

Pyro-Collodion.—The terms **pyro-collodion** and **collodion cotton** are used to designate lower nitrates of cellulose containing about 12.6 per cent. nitrogen, more or less soluble in alcohol-ether and used in the manufacture of smokeless powders.

Gun Cotton.—Finally the highest nitrates of cellulose, containing about 13.4 per cent. nitrogen and probably the *tri-nitrate*, constitute the explosive known as **gun-cotton**, **explosive cotton** or **ballistic cotton**. They are practically insoluble in alcohol-ether.

Celluloid.—One of the most interesting products made from the cellulose nitrates is **celluloid**. When **pyroxylin** is mixed in definite proportions with **camphor** in the presence of alcohol a dough-like mass is obtained which when subjected to heat and pressure forms a homogeneous product that when cold is hard and brittle but when hot is plastic. It is thus able to be molded into various shapes or it may be cut or sawed and polished. In thin sheets it is transparent but is opaque in thick pieces. It may be made more opaque by the addition of zinc oxide or similar inert substances and it may be dyed or colored with pigments. By various treatments celluloid is thus possible of use in a great variety of ways and many toilet articles, novelties and other products are common forms in which it is known. From it very good imitations of ivory, tortoise shell, onyx, window glass, etc., are made and widely used. Its disadvantage is its inflammability which, though diminished by addition of mineral substances, has never been wholly prevented.

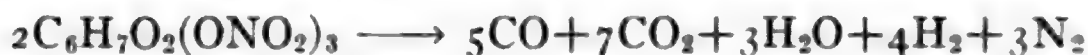
Cellulose Explosives.—The explosives made from cellulose are of two kinds, viz., **cellulose nitrates** alone, as in **gun cotton**, and mixtures of **cellulose nitrates** and **nitro-glycerol** which constitute the **smokeless powders** made from cellulose nitrates.

Gun Cotton.—As nitric acid esters of poly-hydroxy alcohols, the two important explosives **nitro glycerol** and **gun cotton** are exactly analogous not only in character but also in the fact that each is the

fully nitrated product of the alcohol compound from which it is made. Considered as the cellulose tri-nitrate gun cotton has the empirical formula $C_6H_7O_2(ONO_2)_3$.

Nitration.—In the nitration process for the manufacture of the various cellulose nitrate products, whether as **pyroxylin**, **pyro-collodion** or **gun cotton**, cellulose in the form of purified and dried cotton, usually cotton waste, though in some cases, as in making pyroxylin for celluloid, tissue paper is used, is treated with a *mixture of nitric and sulphuric acids*. The proportions and concentrations of the acids and the length of time and temperature of the nitration, while definite for each product, vary considerably according to the degree of nitration desired. In the ordinary process known as *dipping*, the cotton is immersed in the acid bath for about ten minutes, then removed from the bath and, while wet with the acid, placed in earthen pots which are kept cold. The digestion in these pots continues for about twelve hours, in the case of gun cotton, after which the cotton is placed in a centrifuge and the greater part of the acid removed. In another process the nitration is carried on in the centrifuge. In the **Thomson displacement process** the cotton is placed in the acid bath and allowed to remain for about two hours. Cold water is then allowed to flow in slowly at the top while the acid is withdrawn at the bottom. After about three hours the water replaces the acid almost completely and without heat. As either gun cotton or any of the other products must be definite in respect to nitrogen content frequent control analyses are necessary at the first, until the conditions of nitration are fixed. After the nitrated cotton is centrifuged it is thoroughly washed and boiled. Before boiling the gun cotton is fibrous, of the same general character as the original cotton. The boiling not only removes the last traces of acid but the fibrous material is converted into a pulp or colloidal product which is more stable. After boiling the gun cotton is drained of most of the water leaving a product containing about 25 per cent. water. For use in mine cartridges and torpedoes the moist gun cotton is compressed, by which treatment it is made safer and more powerful in its explosive force. Gun cotton is *soluble* in **benzene**, **ethyl acetate**, **acetone** and **nitro benzene** but is *insoluble* in **water**, **alcohol**, **ether**, **acetic acid** or in **nitro glycerol**. It is an extremely strong, shattering, non-propelling explosive and when moist or compressed is usually exploded by means of a *detonator* of dry gun cotton which is ignited by a *fulminating cap*.

When unconfined and ignited it burns rapidly but without explosion. The decomposition products of either burning or explosion are **carbon mon-oxide**, CO, **carbon di-oxide**, CO₂, **water**, H₂O, **hydrogen**, H₂, and **Nitrogen**, N₂. It is therefore smokeless



1 *kilogram* of gun cotton yields 741 *liters* of gas at ordinary temperatures or 982 *liters* if the temperature is above the boiling point of water. The chief uses of gun cotton as such are in *torpedoes*, *grenades* and *mine cartridges*, though for military purposes it is now largely replaced by other high explosives such as **tri-nitro toluene**, T.N.T., and **tetryl** (see Part II).

Cordite, Smokeless Powders, etc.—While gun cotton is insoluble in nitro glycerol, when the two are mixed and treated with acetone and a little vaseline, a gelatinous paste is obtained which is known as **cordite**. This is one of the smokeless powders made from nitro celluloses and possesses propelling properties unlike gun cotton. The first smokeless powder was made by **Vieille**, in 1884, who destroyed the shattering non-propelling action of gun cotton by converting it from a fibrous to a non-fibrous substance, by dissolving the gun cotton and then allowing the solvent to evaporate. Most of the smokeless powders containing nitro celluloses are, however, made from the lower nitrates, pyro-collodion, and not from gun cotton. **Collodion cotton** when mixed to the amount of 2–10 per cent. with **nitro glycerol** forms gelatinous products which have lost more or less of the shattering properties of gun cotton and have taken on propelling properties necessary for gun cartridges and shells. The varieties of the products obtained are many depending upon the proportion of collodion and the amount of nitrogen in the collodion. Some are used for blasting purposes while others are used in guns. They are termed in general **gelatin powders**, **blasting gelatins** or **gum dynamites**, the latter containing some absorbent substance like wood meal or sodium nitrate. The first explosives of mixed nitro glycerol and nitro celluloses were made by **Nobel** already referred to in connection with dynamite (p. 202). One of these is known as **ballistite** and consists of about 50 *per cent.* **nitro glycerol** and 50 *per cent.* of **collodion cotton** containing 11.2–11.7 *per cent.* **nitrogen**. All of these smokeless powders and gum dynamites possess advantages over either nitro glycerol or gun cotton and are much used in both military operations and blasting. In the former use, however, they have been more or

less replaced by modern high explosives before referred to. Up to certain limits the *higher the proportion of collodion cotton to that of nitro glycerol the greater is the propelling force and the less the shattering action*. For the purpose of comparison at this time the relative explosive force of some explosives is given.

EXPLOSIVE FORCE OF EXPLOSIVES

Explosive	Wt. of explosive, kilograms	Energy in kilogram-meters
Nitro glycerol.....	1 0	680,000
Explosive gelatine.....	1.0	650,000
Dynamite.....	1.0	500,000
Gun cotton.....	1.0	456,000
Potassium picrate.....	1.0	330,000
Mercury fulminate.....	1.0	170,000
Nitrogen chloride.....	1.0	144,000

The preceding discussion of the industrial products obtained from cellulose while not complete nor in technical detail emphasizes the striking fact that cellulose, a widely distributed natural substance, complex in its constitution and inactive in its properties, may, by either mechanical treatment or chemical reaction, be converted into such important products as thread, string and rope; wearing apparel (cotton and linen), Mercerized cotton, artificial silk; collodion, celluloid, smokeless powders and high explosives.

Dextrin, Glycogen, Inulin

Dextrin.—The three poly-saccharoses, **dextrin**, **glycogen** and **inulin** are all compounds possessing the same empirical formula as **starch**, viz., $(C_6H_{10}O_5)_x$. **Dextrin** results from the diastase hydrolysis of starch and on that account is believed to have a constitution that is less complex than that of starch. It is found together with starch and sugar in plants and in vegetable juices. It is prepared by hydrolyzing starch with either diastase or acids. Several forms or varieties are known, or have been found by distinct tests to result, as intermediate products, in the hydrolysis of starch to maltose (p. 364). It is soluble in water, reduces Fehling's solution, and reacts with phenyl hydrazine. In regard to these two reactions, however, there is some question as it is doubtful if the reactions have been obtained with absolutely pure substance. One of the varieties of dextrin gives a red color with an iodine solution. On this account it is known as **erythro-dextrin**. Other

varieties give no color with iodine and are known as **achroo-dextrins**. Dextrin is *not fermented* by *zymase* but is *hydrolyzed by diastase* yielding **maltose**. By the complete hydrolysis, by means of acids, dextrin yields **glucose**. The natural plant gums are probably related to dextrin in regard to the complexity of the molecule. The gums yield, mostly, **pentose** sugars on hydrolysis, *i.e.*, they are **pentosans**, whereas dextrin yields glucose and may be termed a **hexosan**.

Glycogen.—As previously stated starch does not occur in animals. **Glycogen**, however, which is isomeric with starch, does occur in animals and on this account it is known as **animal starch**. It is found in the *liver* and *muscles* of animals where it is present as a reserve food material analogous to starch in plants. It is built up (anabolized) in the animal from the hexose mono-saccharose products of the digestion of carbohydrate food. It is present in the liver to as much as 10 per cent of its weight and in muscular tissue to about 2 per cent. When it is used by the animal as food it is again split into glucose, probably by an enzyme termed **glycogenase**. The glucose then enters the blood circulation and is carried to the cells where it is oxidized with the production of energy. Glycogen is a white amorphous powder soluble in water. It is *dextro* rotatory and is colored brown with iodine. By acid hydrolysis it yields **dextrin**, then **maltose** and finally **glucose**.

Inulin.—**Inulin** is found in certain plants, especially in the tubers of the *Dahlia*. It is isomeric with the other poly-saccharoses and is also a reserve food material. It is a white powder soluble in water. It is *levo* rotatory and gives no color with iodine. It is not hydrolyzed by diastase but by a particular enzyme known as **inulase**. Its peculiar characteristic is that by acid hydrolysis it yields only **fructose**.

Mannans and Galactans

Two other **hexosan** poly-saccharoses resembling starch and cellulose should be mentioned. **Mannans** are polysaccharoses which on hydrolysis yield **mannose**. They are present in **vegetable ivory**. **Galactans** are similar polysaccharoses which yield **galactose** on hydrolysis. The substance known as **agar-agar** is a galactan. Both of these poly-saccharoses are associated in small amounts with cellulose in many plants, *e.g.*, in wheat and other cereals, and in numerous seeds, especially legumes.

The following tabular summary of the carbohydrates may be of value.

TABLE XVII.—SUMMARY OF THE CARBOHYDRATES

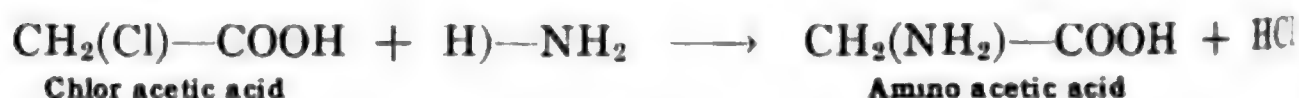
Name	Composition formula	Structural formula, aldehyde or ketone	Stereo-chemical configuration D.L. In.	Optical activity D.L.	Fehling's solution reaction	Phenylhydrazine reaction	Alcoholic fermentation by yeast	Enzyme hydrolyzing	Products of enzyme hydrolysis	Products of acid hydrolysis
Glycerose.....	$C_3H_6O_3$	Ald. + Ket.	In.	In.	+	+	+	—	—	—
Erythrose.....	$C_4H_8O_4$	Ald.	D. & L.	In.	+	+	—	—	—	—
Arabinose.....	$C_5H_{10}O_5$	Ald.	D. & (L.)	D.	+	+	—	—	—	—
Xylose.....	$C_5H_{10}O_5$	Ald.	(D.) & L.	D.	+	+	—	—	—	—
Rhamnose.....	$C_6H_{12}O_6$	Ald.	D. ?	D.	+	+	—	—	—	—
Glucose.....	$C_6H_{12}O_6$	Ald.	D. & (L.)	D.	+	+	+	—	—	—
Fructose.....	$C_6H_{12}O_6$	Ket.	D. & (L.)	L.	+	+	+	—	—	—
Galactose.....	$C_6H_{12}O_6$	Ald.	D. & (L.)	D.	+	+	+	—	—	—
Sucrose.....	$C_{12}H_{22}O_{11}$	Neither	D.	D.	—	—	—	Sucrase (Invertase)	Glucose Fructose	Glucose Fructose
Lactose.....	$C_{12}H_{22}O_{11}$	Ald.	D.	D.	+	+	—	Lactase	Glucose Galactose	Glucose Galactose
Maltose.....	$C_{12}H_{22}O_{11}$	Ald.	D.	D.	+	+	—	Maltase	Glucose	Glucose
Raffinose.....	$C_{18}H_{32}O_{16}$	D.	—	—	—	?	?	Glucose Fructose Galactose
Starch.....	$(C_6H_{10}O_5)_x$	—	—	—	Diastase Ptyalin	Maltose	Glucose
Cellulose.....	$(C_6H_{10}O_5)_x$	—	—	—	Cellulase or cytase	Mannose Galactose	Glucose
Glycogen.....	$(C_6H_{10}O_5)_x$	—	—	—	Glycogenase	Glucose	Glucose
Dextrin.....	$(C_6H_{10}O_5)_x$	—	—	—	Diastase	Maltose	Glucose
Inulin.....	$(C_6H_{10}O_5)_x$	—	—	—	Inulase	Fructose	Fructose

XI. AMINO ACIDS AND PROTEINS

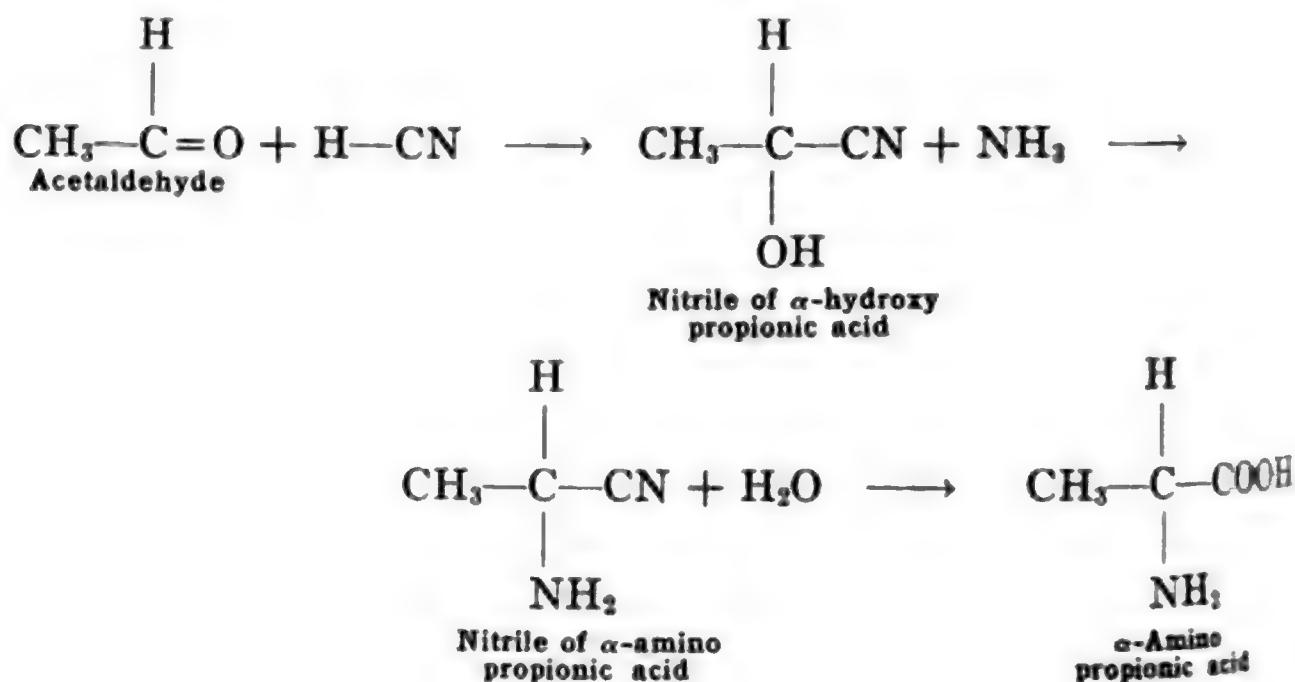
A. AMINO ACIDS

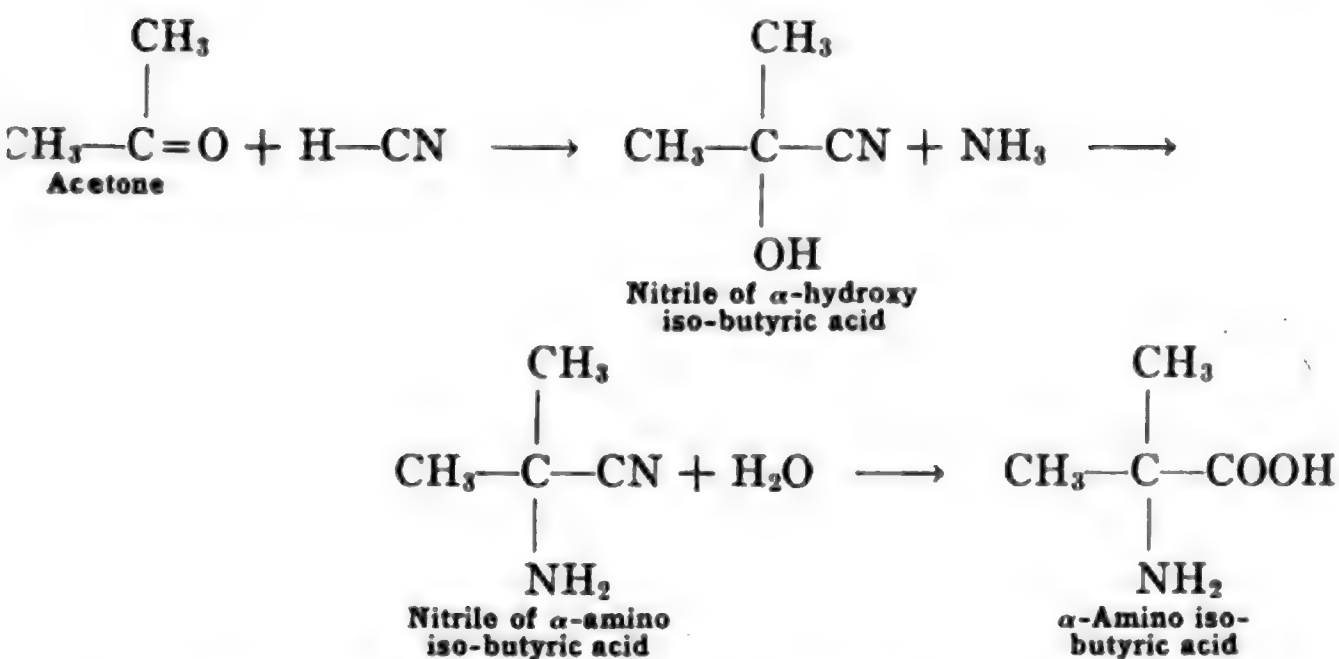
The **amino acids** like the hydroxy acids and the halogen acids belong to the class of substituted acids. In them an *amino group* ($-\text{NH}_2$) is substituted in the non-carboxyl part of the acid. They were not discussed with the other substituted acids because we wished to consider at one time both the amino acids derived from mono-basic acids and those derived from di-basic acids in connection with the proteins which we shall find are related compounds.

Synthesis from Halogen Acids.—The simplest method for the synthesis of amino acids is by the action of ammonia on the halogen acids and is exactly analogous to the formation of alkyl amines from alkyl halides.



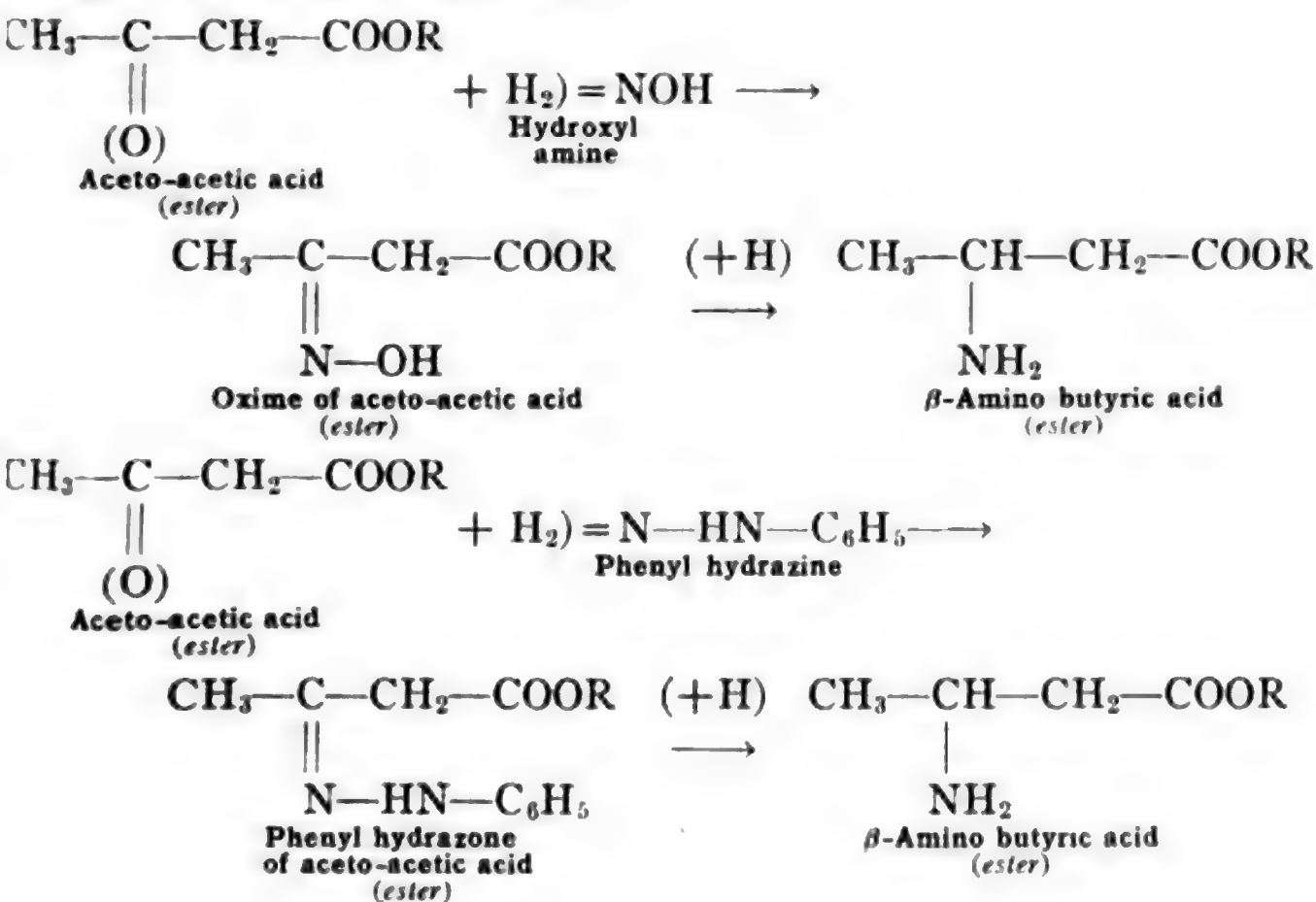
From Aldehydes.—Aldehydes and ketones by the hydrogen cyanide reaction yield cyan-hydrine compounds which are *nitriles* of hydroxy acids. When such an hydroxy acid nitrile is treated with ammonia the hydroxyl group is replaced by the amino group forming the nitrile of the amino acid, the amino acid itself being obtained on hydrolysis of the nitrile.





By this synthesis, it will be noticed that the *alpha*-amino acids result as the amino group is always linked to the carbon to which the carboxyl is also linked. The amino acid will also contain one more carbon than the aldehyde or ketone due to the addition of the cyanide radical, i.e., **acetic aldehyde** yields **amino propionic acid** and **propanone (acetone)** yields **amino iso-butyric acid**.

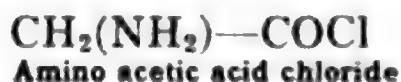
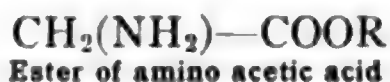
From Oximes and Hydrazones.—The oximes and hydrazones obtained from ketone acids yield amino acids on reduction with sodium amalgam and glacial acetic acid.



By this synthesis the *alpha*-ketone acids yield *alpha*-amino acids and the *beta*-ketone acids yield *beta*-amino acids, etc., and there is *no increase* in the number of carbons in the chain.

From Proteins.—The most important method of preparing amino acids is not a true synthesis but a splitting of complex compounds. This is the *hydrolysis of proteins* which will be discussed a little later. The amino acids are of especial importance because they are directly connected with the living processes of plants and animals through the protein constituents. They are formed from the proteins by enzymatic or bacterial fermentation or by acid hydrolysis. They are crystalline compounds readily soluble in water, usually possessing a sweet taste. In their general character they resemble the hydroxy acids reacting readily and thus lending themselves to investigation.

Acid and Basic.—As the amino acids contain both an *amino group* and a *carboxyl group* they react *both as acids and as bases*. In this double rôle they exhibit very interesting properties. This same double character of acid and base has also been referred to in connection with the hydroxy acids. In this case the basic character is due to the presence of an *alcoholic hydroxyl group* and is consequently *weak*. With the amino acids, however, the basic character is due to the presence of the *much more basic amino group* so that the double acid and basic character of the compounds is *more pronounced*. As acids the amino acids yield *esters* and *acid chlorides*.

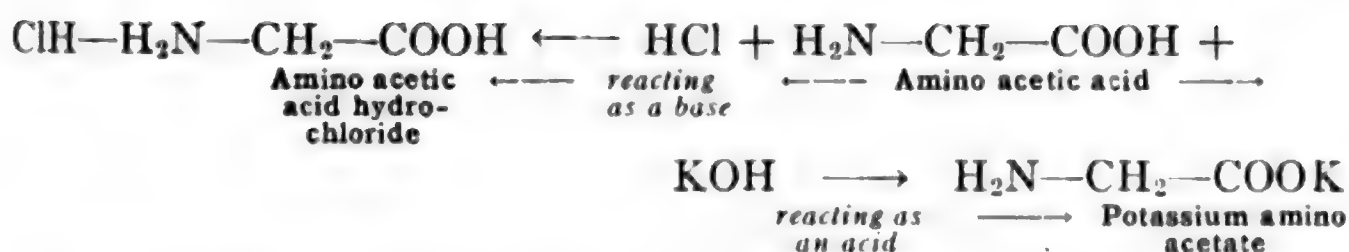


Esters.—The esters are of interest because it has been through them that the separation of amino acids obtained by the hydrolysis of proteins has been accomplished.

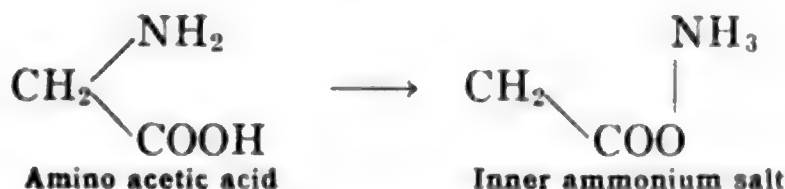
Primary Amines.—As primary amines the amino acids react with nitrous acid in the distinctive way (p. 60) and the amino group is replaced by the hydroxyl group yielding the corresponding *hydroxy acid*.



Salts.—The most interesting and important derivatives of the amino acids are the *salts*. Reacting *as an alkyl amine* they yield salts with *acids* and *as an acid* they form salts with *bases*.



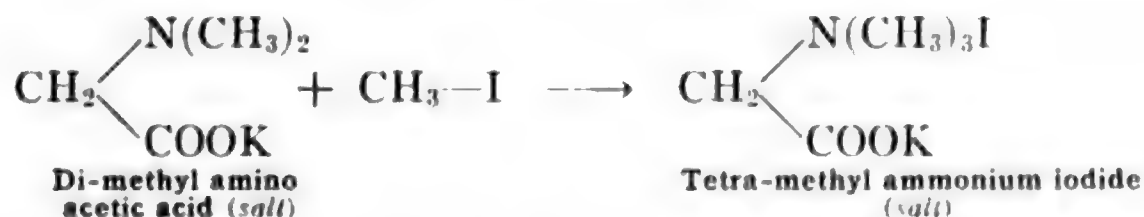
Inner Salts.—We would also expect *inner salts* to be formed in which the basic amino group neutralizes the acid carboxyl group *in the same molecule*.



The existence of such an inner salt is well established by the physical properties of many amino acids and by the chemical reactions of the higher alkylated amino derivatives formed by converting the *primary* amine group into *secondary* and *tertiary* alkyl amine groups.

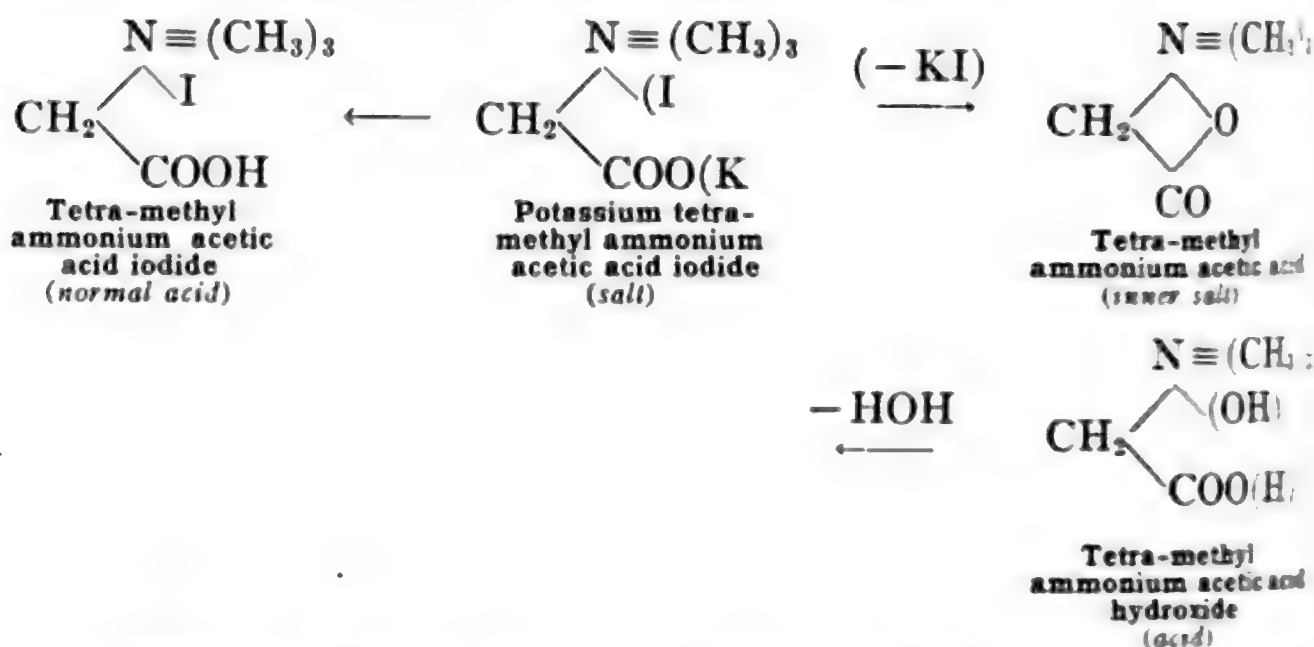


The *tertiary* amine group in this last compound being *more strongly basic* than the primary amine group in amino acetic acid would more readily form an inner ammonium salt. There is also a tetra-methyl ammonium iodide compound formed analogous to the tetra-methyl ammonium salts of the alkyl amines.

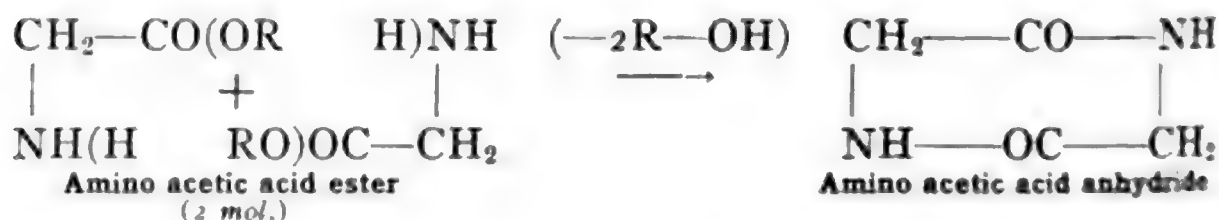


With acids this salt loses potassium iodide, KI, and yields an acid. This acid has the constitution of an inner salt and would be related to what we may term the normal tetra-methyl ammonium iodide acid, by the loss of hydrogen iodide, and to a tetra-methyl ammonium

hydroxide compound, by the loss of water, *i.e.*, as an anhydride. These relationships may be represented as follows

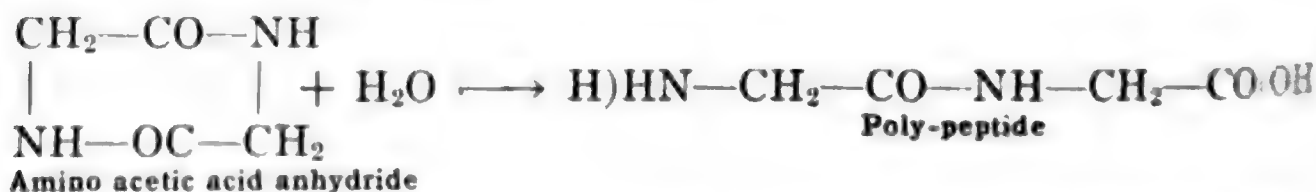


Anhydrides, Di-keto-piperazines.—By far the most important derivatives of amino acids are the *anhydrides* and a related group known as *poly-peptides*. When the ester of an amino acid is prepared it readily loses two molecules of alcohol and yields a *double anhydride*. Such an anhydride is not an inner compound like the one above as water or alcohol is lost by the interaction of two molecules of the acid or the ester as follows.



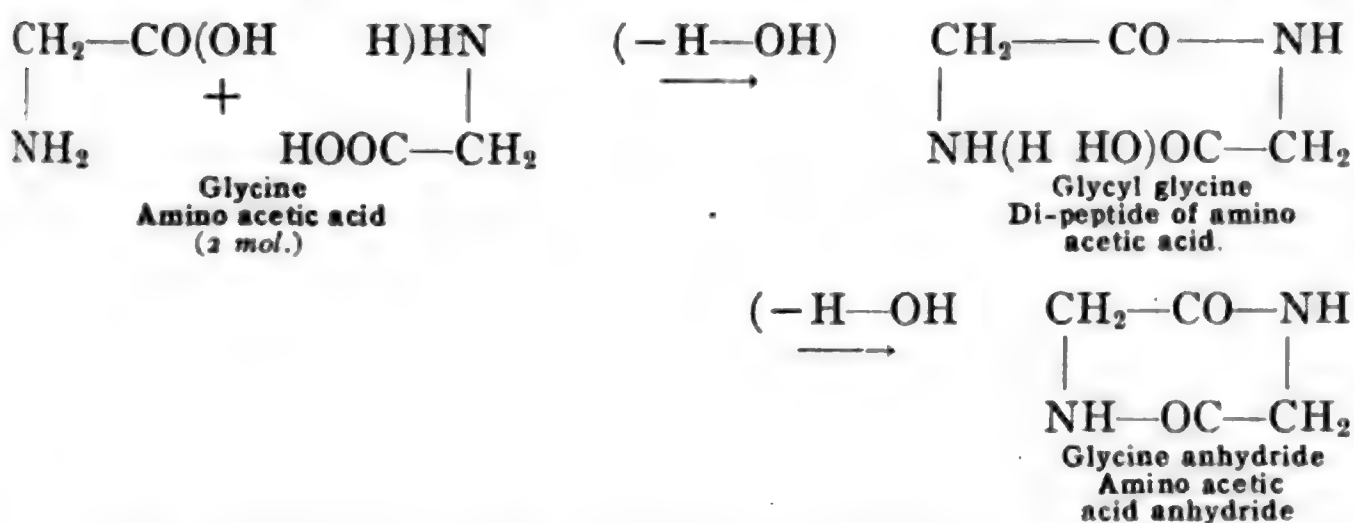
These anhydrides are known as *di-keto piperazines*.

Polypeptides.—When these anhydrides are treated with dilute alkali, **Emil Fischer** found that one molecule of water is restored, the compound resulting being as follows:



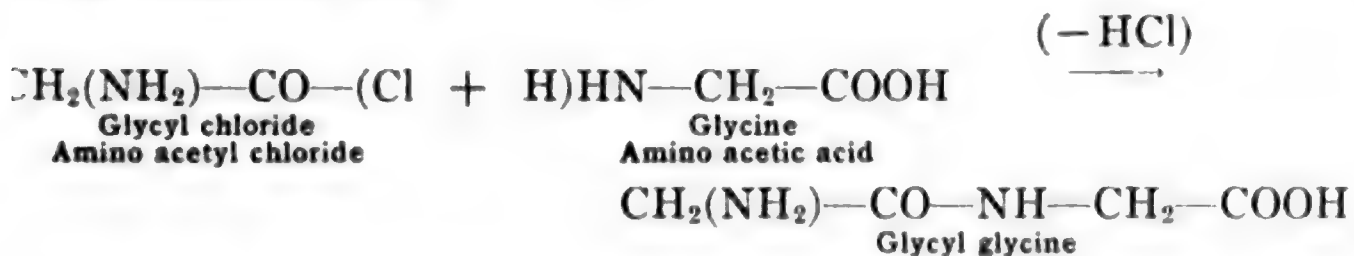
These new compounds **Fischer** called **peptides** or **poly-peptides**, as they are made up of *two or more molecules of an amino acid*. This poly-peptide or **di-peptide** of amino acetic acid, which would be called

amino aceto amino acetic acid, is better termed **glycyl glycine**, **glycine** being another name for amino acetic acid. These poly-peptides form the connecting link between simple compounds like amino acetic acid and the very complex proteins. We shall discuss this presently. Plainly a di-peptide, where it has two residues of the same amino acid, is intermediate between the amino acid and the amino acid anhydride, being the single anhydride of the amino acid.



This formation of single and double anhydrides from two molecules of an amino acid by loss of first one and then a second molecule of water is exactly analogous to the similar formation of anhydrides in the case of hydroxy acetic acid and all *alpha* hydroxy acids (p. 241).

This dipeptide bears to amino acetic acid a relationship similar to that which aceto acetic acid bears to acetic acid. This is indicated by the name **amino aceto amino acetic acid**. Another method of preparing the polypeptides is by the action of the *acid chloride* of the amino acid on the *amino acid* itself.



In the list of amino acids which follows there are included all that have been obtained as products of protein hydrolysis and which are therefore necessary to consider in connection with the constitution of proteins. Most of them are derivatives of acids, which we have already studied though several of them contain *cyclic* or **benzene** groups derived from compounds which we shall take up in Part II.

It will be unnecessary to give the properties or the derivatives of the different acids except in a few cases where the derivatives are individually important. The general facts which have just been discussed apply to all.

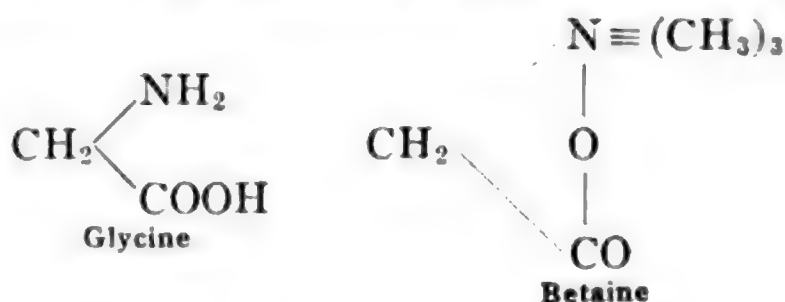
I. MONO-AMINO ACIDS DERIVED FROM MONO-BASIC ACIDS

Glycine, $\text{CH}_2(\text{NH}_2)\text{—COOH}$, Amino Acetic Acid

This acid is also called **glycocoll** but the name **glycine** is better as it indicates the *amine* character of the compound. The termination *ine* has been generally accepted for the names of all amino acids. A few derivatives of glycine are important.

Sarcosine, $\text{CH}_2(\text{NHCH}_3)\text{—COOH}$, **Methyl amino acetic acid**, is the mono-methyl derivative. It is obtained from natural substances, viz., from **creatine**, found in muscular tissue, and from **caffeine**, found in coffee.

Betaine is the **tetra-methyl ammonium inner salt** compound already referred to (p. 386). It is really a tri-methyl derivative of glycine.



It is found in the beet-root and remains in beet sugar molasses. It is the source for the commercial preparation of **tri-methyl amine** which it yields on distillation. It will be referred to again in connection with the **alkaloids** (Pt. II).

Hippuric acid, $(\text{C}_6\text{H}_5\text{—CO})\text{—NH—CH}_2\text{—COOH}$, **Benzoyl glycine**, is a normal constituent of urine, being abundant in that of herbivorous animals but present in smaller amounts in man. It is a *benzoyl* derivative of glycine, benzoyl being the *acyl* group of a **benzene** acid known as **benzoic acid**, $(\text{C}_6\text{H}_5\text{—CO})\text{OH}$.

It is similar in its constitution to a dipeptide except that one acid constituent has no amino group. A compound exactly analogous to it is **aceto amino acetic acid**, $\text{CH}_3\text{—CO—NH—CH}_2\text{—COOH}$. Such semi-peptides result when an amino acid is treated with the acid chloride of a non-amino acid analogous to the second method of preparing poly-

peptides (p. 387). In urine it is formed from benzoic acid in the food and glycine resulting from the breaking down of protein in the body.

Di-amino Acetic Acid, $\text{CH}(\text{NH}_2)_2\text{—COOH}$

This acid has also been obtained as a hydrolytic product of proteins.

Alanine, $\text{CH}_3\text{—CH}(\text{NH}_2)\text{—COOH}$, α -Amino Propionic Acid

The next higher acid to acetic, viz., propionic acid, yields an *alpha*-amino acid known as **alanine**. There has also been isolated from muscle a *beta*-amino propionic acid, $\text{CH}_2(\text{NH}_2)\text{—CH}_2\text{—COOH}$.

Serine, $\text{CH}_2(\text{OH})\text{—CH}(\text{NH}_2)\text{—COOH}$, α -Amino β -Hydroxy Propionic Acid

This acid is obtained from silk protein. It is also called **hydroxy alanine**.

Cysteine, $\text{CH}_2(\text{SH})\text{—CH}(\text{NH}_2)\text{—COOH}$, α -Amino β -Sulph-hydro Propionic Acid

This acid is the sulphur analogue of **serine**.

Cystine, $\text{HOOC—CH}(\text{NH}_2)\text{—CH}_2\text{—S—S—CH}_2\text{—CH}(\text{NH}_2)\text{—COOH}$

This acid is a **di-cysteine** resulting from two molecules of cysteine by the loss of two hydrogen atoms from the sulph-hydro groups, (—SH). It is found in urinary calculi.

Phenyl Alanine, $\text{C}_6\text{H}_5\text{—CH}_2\text{—CH}(\text{NH}_2)\text{—COOH}$, α -Amino β -Phenyl Propionic Acid

This amino acid, as its name indicates, is the phenyl derivative of alanine. The radical **phenyl**, ($\text{C}_6\text{H}_5\text{—}$), is from the hydrocarbon **benzene**, C_6H_6 .

Tyrosine, $(\text{C}_6\text{H}_4\text{OH})\text{—CH}_2\text{—CH}(\text{NH}_2)\text{—COOH}$, α -Amino β -(Hydroxy-phenyl) Propionic Acid

This acid is closely related to the preceding one. It is **hydroxy-phenyl alanine**, the group ($\text{—C}_6\text{H}_4\text{OH}$) being substituted in the *beta* carbon group of alanine. Tyrosine is of especial interest as it was one of the first amino acids to be obtained from proteins. It can be easily obtained from cheese.

Tryptophane, $(\text{C}_8\text{H}_6\text{N})\text{—CH}_2\text{—CH}(\text{NH}_2)\text{—COOH}$, α -Amino β -Indol Propionic Acid

This is an amino acid the name of which does not have the *ine* termination. The *beta* carbon group in alanine has substituted in it the complex group, ($\text{C}_8\text{H}_6\text{N}$), which is known as the *indol* radical. **Indol** is a benzene derivative related to **indigo**. Tryptophane derives its name

from the fact that it was first obtained in the digestive products of protein by **trypsin**, the proteolytic enzyme of the pancreatic juice.

Histidine, $(C_3H_3N_2)-CH_2-CH(NH_2)-COOH$, α -Amino β -Imidazol Propionic Acid

This is another amino acid containing a cyclic radical substituted in the *beta* carbon group of alanine.

α -Amino Butyric Acid, $CH_3-CH_2-CH(NH_2)-COOH$

This amino acid is the only one which is a derivative of butyric acid, the four carbon member of the fatty acid series. It has no special name.

Valine, $CH_3-CH-CH(NH_2)-COOH$, α -Amino Iso-valeric Acid
 $\quad \quad \quad |$
 $\quad \quad \quad CH_3$

Iso-valeric acid is one of the isomeric five carbon acids. It is *3-methyl butanoic acid*. Valine is the *alpha*-amino derivative of it.

α -Amino Valeric Acid, $CH_3-CH_2-CH_2-CH(NH_2)-COOH$

There has also been isolated from the products of protein hydrolysis the *alpha*-amino derivative of the normal five carbon acid, **valeric acid**. It has no special name.

Leucine, $CH_3-CH-CH_2-CH(NH_2)-COOH$, α -Amino β -Iso-propyl Propionic Acid
 $\quad \quad \quad |$
 $\quad \quad \quad CH_3$

The amino acid leucine is an *alpha*-amino derivative of one of the other isomeric six carbon acids, viz., *4-methyl pentanoic acid*, as is shown in the above formula.

Iso-leucine, $(CH_3-CH_2)-CH-CH(NH_2)-COOH$, α -Amino β -Ethyl β -Methyl Propionic Acid
 $\quad \quad \quad |$
 $\quad \quad \quad CH_3$

This amino acid, as the name indicates, is isomeric with leucine. It is the *alpha*-amino derivative of another of the isomeric six carbon acids, viz., *3-methyl pentanoic acid*.

Caprine, Glyco-leucine, $CH_3-CH_2-CH_2-CH_2-CH(NH_2)-COOH$, α -Amino Caproic Acid

Caprine is the *alpha*-amino derivative of the normal six carbon acid or **caproic acid**. Its name **glyco-leucine** indicates its relation to glucose and to leucine.

II. DI-AMINO ACIDS DERIVED FROM MONO-BASIC ACIDS

Arginine, $(\text{H}_2\text{N}-\text{C}(\text{NH})-\text{NH})-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}(\text{NH}_2)-\text{COOH}$, α -Amino δ -Guanidine Valeric Acid

Arginine and **lysine** are amino acids which differ from those preceding in having *two* amino groups. In arginine one of the amino groups is part of a complex radical of a compound known as **guanidine**, $\text{H}_2\text{N}-\text{C}(\text{NH})-\text{NH}_2$, which is related to **urea** and will soon be discussed. Arginine is a derivative of the normal five carbon acid known as **valeric acid** having one amino group in the *alpha* position and the guanidine radical, containing the second amino group, in the end carbon group or *delta* position.

Lysine, $\text{CH}_2(\text{NH}_2)-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}(\text{NH}_2)-\text{COOH}$, α - ϵ -Di-amino Caproic Acid

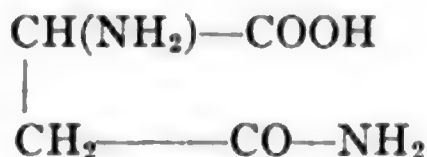
The other *di-amino* acid derived from mono-basic acids is known as **lysine**. It corresponds to the mono-amino acid, glyco-leucine. Both are derived from the normal six carbon acid, **caproic acid**.

III. MONO-AMINO ACIDS DERIVED FROM DI-BASIC ACIDS

$\text{CH}(\text{NH}_2)-\text{COOH}$
 Aspartic Acid, , Amino Succinic Acid
 CH_2-COOH

This amino acid is the mono-amino derivative of the di-basic **succinic acid**.

Asparagine is an important derivative of aspartic acid. It is the *mono-acid-amide*, viz.,



Asparagine is found in several plants, especially in *asparagus*, from which both it and aspartic acid derive their names. While it contains two amino groups it is not a di-amine as one amino group is in the *acid amide* grouping.

Glutamine, **Glutaminic Acid**, $\text{HOOC}-\text{CH}_2-\text{CH}_2-\text{CH}(\text{NH}_2)-\text{COOH}$, α -Amino Glutaric Acid

The next higher di-basic acid to succinic acid, viz., **glutaric acid**, yields an amino acid known as **glutamine**, **glutaminic acid**, or **glutamic acid**. It occurs more widely distributed than any of the other amino acids. Most proteins yield larger amounts of it than of any other

amino acid. In the group of proteins known as **protamines** it is wholly absent in the hydrolytic products.

Proline, $C_4H_7N-COOH$, α -Pyrrolidine Carboxylic Acid

This compound is not a simple amino acid but is a carboxyl derivative of a five membered cyclic compound, containing an ($-NH-$) group, known as **pyrrolidine** (p. 194 and Part II).

Oxy-proline, $(C_4H_7(OH)N)-COOH$, α -(Hydroxy Pyrrolidine) Carboxylic Acid

As its name indicates oxy-proline is an hydroxy derivative of proline. The position of the hydroxyl group in the pyrrolidine ring is not known.

Di-amino Di-hydroxy Suberic Acid, $C_8H_{14}N_2O_4$

Di-amino Tri-hydroxy Dodecanoic Acid, $C_{12}H_{24}N_2O_6$

These two amino acids can be given by name and empirical formula only, as their full constitution is unknown. The first is a derivative of the eight carbon di-basic acid known as **suberic acid**, $HOOC-(CH_2)_6-COOH$. The second is derived from the twelve carbon mono-basic acid, *dodecanoic acid*, $CH_3(CH_2)_{10}-COOH$.

The foregoing description is little more than a catalogue list but it shows that the amino acids related to proteins are in most cases derivatives of well known *mono-* and *di-basic aliphatic acids* and that at least one nitrogen in every case except in proline and oxy-proline is in the form of a simple amino group substituted in the acid, usually in the *alpha* position. Six of the number contain also more or less complex cyclic groups substituted in the aliphatic acid and four of these cyclic groups contain nitrogen in the *imino grouping* ($=NH$). Proline and oxy-proline have no simple amino group. Taken as a whole, therefore, both as to their number and constitution, the amino acids form a rather complex group and indicate how complex must be the constitution of the proteins from which they are derived. More detailed discussion of the properties of the individual acids and the amounts in which they are obtained by the hydrolysis of different proteins may be found in larger books on biochemistry and physiological chemistry.

B. PROTEINS

Proteins like fats and carbohydrates are substances of great biological importance. All three are essential organic constituents of every living cell. The most common examples of proteins are such substances as the white of egg, **egg albumin**; the gummy substance in wheat

wheat gluten; and the curd of milk, **casein**. The chemical term protein has a similar significance to the biological term *protoplasm* for both names have reference to the primary or fundamental nature of the substances, protein meaning *to be first* and protoplasm *first form*. The two are not, however, synonymous or equivalent terms for it has been shown that while protein is an essential constituent of cell protoplasm it is not the only one, for both carbohydrates and fats, together with certain inorganic salts, are also always present. Biologically, therefore, **fats, carbohydrates and proteins** are of similar importance and we cannot say that one is more essential to living matter than the other two.

In the development of our knowledge of the chemistry of these biological compounds both the fats and carbohydrates were pretty thoroughly understood long before the proteins. It has been found that in their constitution the fats are relatively simple, the carbohydrates considerably more complex and the proteins the *most complex* of all. In connection with our discussion of the constitution of the carbohydrates we stated that **Emil Fischer** was one of the foremost of the workers in this field and the one who first synthesized a member of the hexose mono-saccharose group (p. 340). It is especially interesting that one who did so much to establish our knowledge of one group of the essential constituents of living matter should later turn his attention to the remaining unsolved constituent and in a most wonderful way clear up the whole matter. We do not mean that he alone solved this problem for many others have made most important contributions to the subject. In addition to **Fischer**, the names of **Conheim, Kossel, Kütscher, Thomas B. Osborne** of the New Haven Experiment Station, and above all **Abderhalden**, the student of **Fischer** and co-worker with him, will always be associated with the subject of proteins and the development of our ideas as to their constitution.

Composition.—Proteins differ from the other essential organic constituents of living cells in containing not only carbon, hydrogen and oxygen as carbohydrates and fats do, but in addition to this they always contain the element nitrogen; usually sulphur and sometimes phosphorus, or iron, or one of a few other elements. The proportion of nitrogen in proteins is fairly constant, varying between the approximate limits of 15 per cent and 19 per cent while in most cases it approximates closely the value of 16 *per cent*. This was one of the first facts noted in regard to proteins and has given rise to the universal

use of the *factor* 6.25 for converting per cent nitrogen into per cent protein. In the ordinary agricultural analysis of plant and animal materials the substance is analyzed for nitrogen, usually by the Kjeldahl method, and the nitrogen is converted into protein by means of this factor. $N. (\text{per cent}) \times 6.25 = \text{Protein (per cent)}$. In all older analyses of such substances and when the factor is not otherwise definitely stated this factor is understood.

The complete percentage composition of proteins may be given as follows:

Carbon	51-55	per cent
Hydrogen	6-7	per cent
Nitrogen	15-19	per cent
Oxygen	20-24	per cent
Sulphur	0.3-2.3	per cent
Phosphorus	0.4-0.8	per cent (when present)
Other elements,	traces only (when present)	

Molecular Weight.—While the composition of proteins has been accurately determined it is impossible as yet to assign a molecular formula because in order to do this we must know the molecular weight, and accurate or even acceptable molecular weights have not yet been obtained. Every indication points to the view that the compounds are both exceedingly complex in structure and exceptionally large in their molecular weight. Assuming, in the case of sulphur, iron, or one of the other elements, which are present in very small percentage amounts, that at least one atom of the particular element is present in the molecule, we can calculate the size of the molecule. Determinations made in this way have given results as follows:

Edestin , based on per cent of sulphur present,	molecular weight
	= 14,530
Egg albumin , based on per cent of sulphur present,	molecular weight
	= 15,203
Blood serum albumin (horse), based on per cent of sulphur present,	molecular weight
	= 14,980
Blood oxy-hemoglobin (horse), based on per cent of sulphur present,	molecular weight
	= 16,655
Blood oxy-hemoglobin , based on per cent of sulphur and iron present,	molecular weight
	= 15,000

A molecular formula for oxy-hemoglobin based upon its percentage composition and the molecular weight as given in the last figure, viz., 15,000, is



Such a formula of course means little except to emphasize the fact that we are dealing with compounds of very large molecular weight and consequently of very complex structure seeing that the elements present are few and of relatively small mass.

Physical Properties.—The physical properties of the proteins were the first basis for classifying them into various related groups and for a long time remained our only basis for such classification.

Non-crystalline.—The fact that proteins are *non-crystalline* substances has made the preparation of pure individual compounds practically impossible. We are therefore unable to say whether any so-called individual protein is a true chemical individual or not.

Solubility.—The only physical property which at first gave any indication that individual compounds were obtained is that of solubility, and here too the line of demarkation between two proteins is often very indistinct, as differences in solubility are not sharp, as is often the case with crystalline compounds. Differences in solubility in such reagents as water, alcohol, neutral salt solutions of different concentrations, dilute alkalies, etc., were the basis for the first separation of the proteins into groups. For example, certain proteins like **egg albumin** were found to differ from all others in being *soluble in water*, and proteins of similar solubility found in blood and milk were termed **blood albumin** and **milk albumin**. Proteins of another group were found to be soluble in *dilute neutral salt solutions* but *insoluble in water*; others were *soluble in alcohol*; etc. This illustrates the way in which names and groups became fixed.

Chemical Properties.—In their chemical properties the proteins are characterized by marked inactivity. Largely on account of this property, which prevented their study by the usual methods, practically nothing was known for a long time as to their real chemical nature. Recently the study of the decomposition products obtained by boiling with acids, *i.e.*, the hydrolytic products, has led to the true understanding of them.

Amino Nitrogen.—It was very early recognized that in proteins the nitrogen was probably held in ammonia groupings, *i.e.*, in *amino*, *imino*

or *acid amide* groups and possibly also as *ammonium salts*. Proteins differ as to the proportion of the total nitrogen which is liberated by boiling with magnesium hydroxide or with sodium hydroxide and the action of these different reagents indicates the proportion of each of the several different nitrogen groupings. Magnesium hydroxide was believed to set free as ammonia only such nitrogen as exists in the form of an *ammonium salt*. On the other hand, sodium hydroxide decomposes ordinary *amino acids* and *acid amides* so that nitrogen obtained as ammonia by such treatment was considered as amino acid or acid amide nitrogen. Finally decomposition with sulphuric acid and subsequent distillation with sodium hydroxide converts all protein nitrogen into ammonia, or in addition to that obtained by the first two reagents it yields also the strongly basic *di-amino nitrogen*. As a result of this method of study the idea became more generally accepted that the probable combination of the nitrogen of proteins is as *amino nitrogen* in its different forms and usually in that of an *amino acid*.

Hydrolysis of Proteins.—Then it was found that by boiling proteins with dilute acids certain of the simpler amino acids were obtained as final hydrolytic products. This led to the study of proteins in respect to the various amounts of the different amino acids which are obtained on hydrolysis. For example, **gliadin**, one of the proteins of wheat gluten, yields an exceedingly large amount, 43.66 *per cent* of **glutamine** and only 3.16 *per cent* of **arginine**; while **salmine** yields *no glutamine* but a *very large amount*, 89.20 *per cent*, of **arginine**.

Simple Proteins.—Proteins have also been grouped according to the apparent complexity of the molecule. Certain ones like the albumins seem to possess a simpler character than others and are therefore called *simple proteins*.

Conjugated Proteins.—Another group of proteins show a more complex character in that some react *both as proteins and also as carbohydrates*. Others show the presence of **nucleic acid**, or **iron** or **phosphorus** in addition to the protein. Such proteins are termed *conjugated proteins*, e.g., **mucin**, a protein of the **saliva**, is a conjugated *carbohydrate-protein*, or, as it is termed, a **glyco-protein**. The **hemoglobin** of the blood is a conjugated *iron-protein* or **hemoglobin**. **Caseinogen**, the protein of milk, which on coagulation yields curd or **casein**, is a conjugated *phosphorus-protein* or **phospho-protein**, etc.

Derived Proteins.—Though generally speaking the proteins are inactive compounds, they are nevertheless changed when acted upon by water, dilute alkalis or acids, and products are obtained still possessing protein characters, but different from the original proteins and in some cases evidently simpler in character. These are termed *derived proteins*. They are of several sub-groups. (A) *Primary derived proteins*, viz., (1) **proteans**, derived from proteins by the simple action of water; (2) **meta proteins**, derived from proteins by action of alkalis or acids; and (3) **coagulated proteins**, derived from proteins by action of heat, e.g., **coagulated egg albumin**. (B) *Secondary derived proteins*, obtained by the action of enzymes and by acid hydrolysis. These are: (1) **proteoses** and **peptones**, which are partial digestion products of proteins by proteolytic enzymes; and (2) **peptides** or **poly-peptides**, the result of more complete enzymatic or acid hydrolysis.

Classification.—As a result of the study of proteins both as to their physical properties, especially solubility and as to their decomposition by acid hydrolysis, a classification of the so-called individual proteins has been accomplished.

Common Proteins.—Before giving the classification it may be well simply to mention some of the more common proteins with the material from which they are obtained:

Egg albumin is white of egg.

Blood albumin and **milk albumin** are similar proteins obtained from the substances indicated.

Blood serum globulin, **egg globulin**, **milk globulin** and **plant globulins**, such as **edestin** from hemp seed and **excelsin** from Brazil nut, are related proteins from the sources indicated.

Glutenin and **gliadin** are the two principal proteins in wheat to which the formation of the **gluten** is due.

Zein, in maize, and **hordein**, in barley, are similar to gliadin.

Collagen is the protein constituent of connective tissue such as *tendons*; **elastin** is in ligaments and **keratin** is in epithelial tissue, such as hoofs, hair, horn, etc.

Globin is the protein part of the conjugated protein **hemo-globin** of the blood.

Salmine, **sturine**, etc., are simple proteins, probably the simplest of all, and are found in fish sperm, e.g., in salmon sperm (**salmine**), and in sturgeon sperm (**sturine**), etc.

Caseinogen is the principal protein of milk to which the formation of the curd is due.

Ovo-vitellin is a similar protein in egg yolk.

Hemo-globin is the conjugated *iron-protein* constituent of red blood corpuscles or really of the coloring matter of the corpuscles.

Classification of Proteins

I. Simple Proteins

1. **Albumins**: egg albumin, blood albumin, milk albumin, and plant albumins.

Soluble in water and coagulated by heat.

2. **Globulins**: egg globulin, edestin, excelsin.

Insoluble in water, soluble in dilute neutral solutions of salts of strong bases and strong acids, *e.g.*, NaCl, $(\text{NH}_4)_2\text{SO}_4$, MgSO_4 .

3. **Glutelins**: glutenin.

Soluble in dilute alkalies or acids. Insoluble in all neutral solvents.

4. **Prolamins**: gliadin, zein, hordein.

Soluble in 70–80 per cent alcohol. Insoluble in water, absolute alcohol or neutral salt solutions.

5. **Albuminoids**: collagen, elastin, keratin.

Insoluble in all neutral solvents.

6. **Histones**: globin (from hemoglobin).

Basic proteins soluble in water and dilute acids, insoluble in ammonia. Yield a large number of amino acids, especially basic or di-amino acids.

7. **Protamines**: salmine, sturine.

The simplest of all proteins, strongly basic, soluble in water, yield few amino acids.

II. Conjugated Proteins

8. **Nucleo-proteins**: cyto-globulin, nucleo-histone.

Contain nucleic acid and protein.

9. **Glyco-proteins**: mucin.

Contain carbohydrate and protein.

10. **Phospho-proteins**: caseinogen, ovo-vitellin.

Contain a phosphorus compound and protein. The phosphorus compound is other than nucleic acid or lecithin.

11. **Hemo-globins** : Hemoglobin (from blood).
Contain an iron compound and protein.
12. **Lecitho-proteins** : contain lecithin and protein.

III. Derived Proteins

(A) *Primary*

13. **Proteans** : myosan, edestan.
These are obtained from proteins by the action of water, very dilute acids or enzymes. Insoluble in water.
14. **Meta proteins** : alkali-albuminates, acid-albuminates.
Obtained from proteins by the further action of dilute alkalies or acids. Soluble in water plus the reagent.
15. **Coagulated proteins** : coagulated egg albumin.
Obtained from proteins by the action of heat or alcohol. Insoluble.

(B) *Secondary*

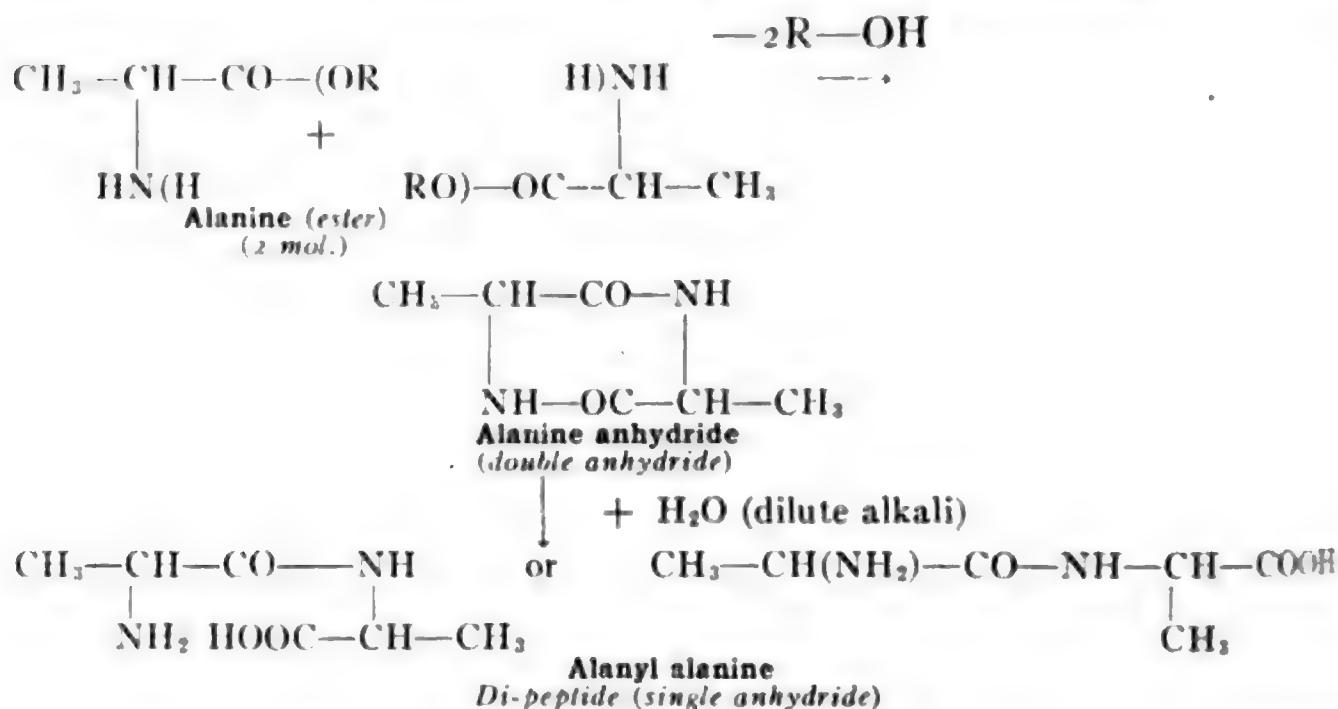
Product of proteolytic hydrolysis or digestion of proteins, also by acid hydrolysis.

16. **Proteoses** :
Soluble in water and not coagulated by heat. Precipitated from solution by saturating it with ammonium sulphate, $(\text{NH}_4)_2\text{SO}_4$ or zinc sulphate, ZnSO_4 .
17. **Peptones** :
Soluble in water, not coagulated by heat and not precipitated from solution by saturation with ammonium sulphate solution.
18. **Peptides or poly-peptides** :
These are not really proteins at all but are compounds of definitely known constitution and which may also be formed by joining together two or more amino acids in the form of single anhydrides (p. 386).

POLY-PEPTIDES AND THE CONSTITUTION OF PROTEINS

There remains to be considered the relation of the **poly-peptides** to the **proteins** and the probable constitution of the proteins. The study of proteins on which the above classification is based has been almost wholly that of their composition and physical properties.

Analytical and Synthetical Study of Proteins.—Fischer attacked the problem of the constitution of proteins from the synthetic side. Assuming that proteins consist of units of amino acids, as indicated by the analytical study of their hydrolytic products, he attempted to synthesize, from amino acids, compounds of similar complexity to the proteins. As already stated (p. 386), he found that the double anhydrides, resulting from the esters of amino acids by the loss of two molecules of alcohol from two molecules of the ester, took up one molecule of water when treated with dilute alkali and a single anhydride was obtained. The reactions may be represented as follows:

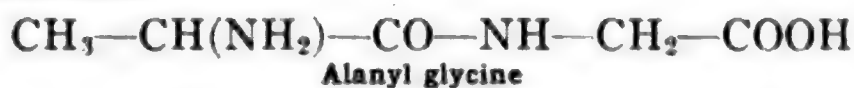
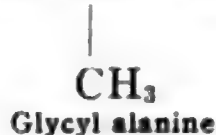


Alanyl Alanine.—From these reactions the resulting compound must have the constitution of a *single anhydride* which would be formed by the union of *two molecules of the amino acid* through the *loss of one molecule of water*, the hydroxyl coming from the carboxyl group of one acid and the hydrogen from the amino group of the other acid. These compounds he termed **peptides** or **poly-peptides**. The one illustrated above is a *di-peptide* formed from two molecules of **alanine**, α -amino propionic acid. It is called specifically **alanyl alanine**. In a wonderfully productive series of investigations he found that a third amino acid can be linked to the di-peptide, through the remaining carboxyl group of the di-peptide and the amino group of the new amino acid, and a *poly-peptide* consisting of *three amino acid units*, i.e., a *tri-peptide*, obtained. Also this linking on of a new amino acid unit can be continued and a large number of such *poly-peptides* actually obtained containing all the way

from *two to eighteen amino acid units*. These amino acid units may be alike, as in the case just given, or different, *e.g.*,



and



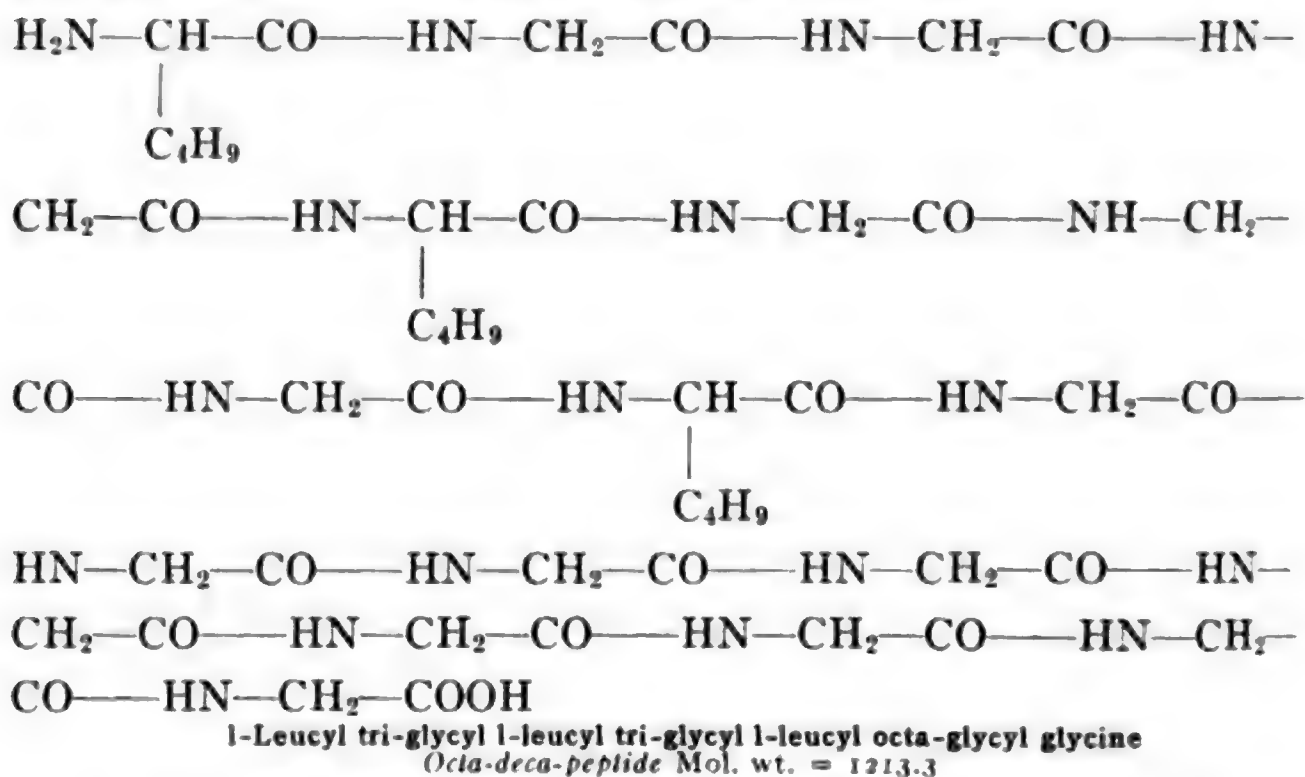
Glycyl Alanine. Alanyl Glycine.—It will be seen at once that a large number of polypeptides are possible of formation from the amino acids which are known and which have been obtained as products of protein hydrolysis.

***alpha*-Amino Acids.**—Two things are prominent in considering the amino acids which have been obtained as hydrolytic products of proteins. *First*, these amino-acids are, in every case except one, *alpha-amino* acids and many of them are derivatives of *alpha-amino* propionic acid. The formation of poly-peptides is therefore natural, as these have the constitution of the particular form of anhydride that is characteristic of *alpha*-hydroxy and *alpha-amino* acids in general (p. 387). *Second*, all of the amino acids, with the exception of glycine, contain an *asymmetric carbon atom*.

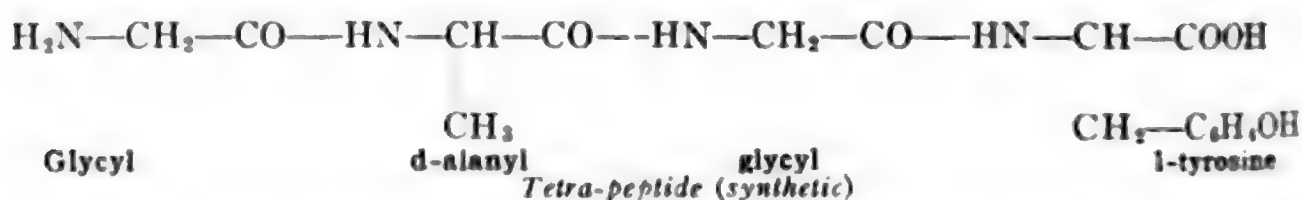
Stereo-isomers.—The compounds thus possess *stereo-isomerism* and exist in the three forms, *viz.*, *dextro* (*d*), *levo* (*l*), and *racemic or inactive* (*i*). In most cases all three of these isomers are known. We can realize at once the exceeding large variety of poly-peptide combinations which are possible among the twenty or more amino acids when these are combined in proportions ranging from di-peptides of two amino acids up to octa-deca-peptides of eighteen amino acids. Each one of the stereo-isomers of each amino acid can also form a poly-peptide union with itself or with any other and also in each case the grouping of any two may be reversed as illustrated by the two di-peptides formed from glycine and alanine, *viz.*, **glycyl alanine** and **alanyl glycine**. The complexity of the molecule and the possibilities of isomeric groupings may be illustrated with the eighteen amino acid poly-peptide, the *octa-deca-peptide*, which has been synthetically prepared. It is composed of *three levo-leucine* units, $(\text{CH}_3)_2 = \text{CH} - \text{CH}_2 - \text{CH}(\text{NH}_2) - \text{COOH}$, or $\text{H}_2\text{N} - \text{CH} - \text{COOH}$, and *fifteen glycine* units, $\text{CH}_2(\text{NH}_2) - \text{COOH}$.



The following formula represents the grouping of these eighteen amino acid units as established by the synthesis of the compound.



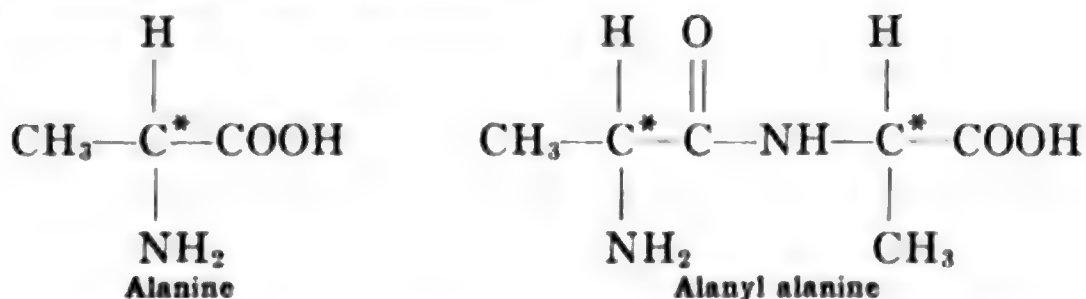
In this compound we have a substance approaching the proteins in complexity and it has been found to resemble the proteins and the proteoses and peptones in its physical properties. Furthermore, a simpler synthetic poly-peptide, viz., a *tetra-peptide*, has been found to be *almost identical* with an isomeric poly-peptide obtained by the hydrolysis of a silk protein. This synthetic tetra-peptide has the following constitution:



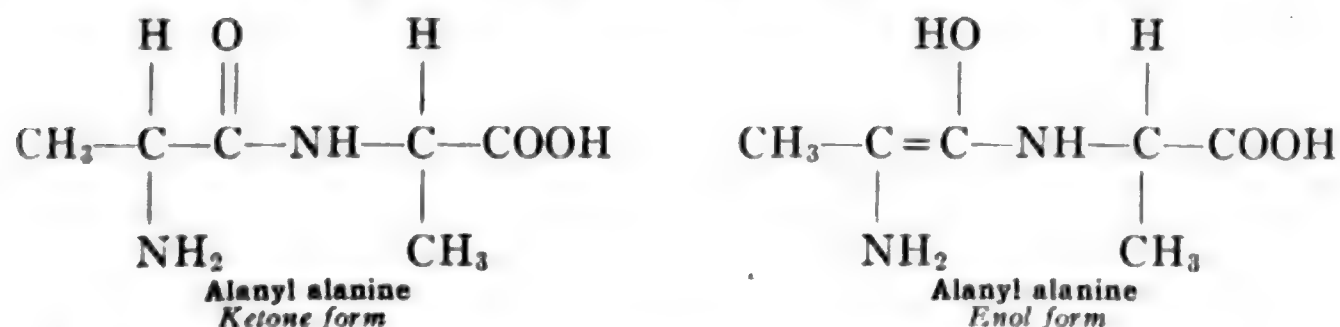
We can easily calculate that, due to different arrangements of the four units, there are *eight* possible isomeric tetra-peptides containing these same four amino acids of the same stereo-isomeric forms. One of these eight isomers *may prove* to be actually identical with the hydrolytic tetra-peptide but it may be necessary to wait until these eight isomers have all been synthesized before we can state *positively* that a *synthetic poly-peptide is identical with a poly-peptide obtained by the hydrolysis of a protein*. The probability is that one of these possible synthetic compounds *will be found to be identical with the hydrolytic*. When this is done we shall have proven that proteins are poly-peptide combinations.

of alpha-amino acids. While the actual proof is yet lacking *there is little doubt that proteins have the constitution of poly-peptides.*

Tautomerism of Poly-peptides and Proteins.—Certain facts seem to indicate that poly-peptide groupings of the amino acids are able to exist in a tautomeric form and that they are converted into this form by the action of alkalis. The poly-peptides, if the constitution assigned them is true, contain the same asymmetric carbon atoms as the amino acids of which they are composed.



The proteins themselves possess optical activity thus supporting the view of their poly-peptide constitution. Now when hydrolyzed by enzymes or by acids the proteins yield amino acids that are *all optically active, i.e.,* either dextro or levo. Usually the total activity of the amino acids obtained is *greater* than that of the original protein. Now when hydrolysis of the protein is effected *by alkalis instead of acids* or when the acid hydrolysis is preceded by treatment of the protein with alkalis it is found that the amino acids obtained are usually of the *racemic or inactive form, i.e.,* there are equal amounts of the dextro and levo forms. Such racemization by the action of alkalis occurs much more readily with the proteins than with the amino acids themselves which indicates that the polypeptide grouping is involved in the change. The explanation given is that alkalis effect a tautomeric rearrangement of the poly-peptide exactly analogous to that occurring in **aceto-acetic ester** (p. 256) and the *ketone* form of the poly-peptide as in the constitution already given is converted into the *enol* form.



In such a rearrangement one of the asymmetric carbon atoms loses its asymmetry and becomes symmetrical. If now this non-asymmetric

amino acid group by hydrolysis of the poly-peptide and formation of the individual amino acid, regains its asymmetric carbon atom which must possess in the amino acid there would be formed equal amounts of the dextro and levo forms and the acid would be obtained in the *racemic inactive form*.

A study of the changes in optical activity due to hydrolysis also makes it possible to determine which amino acid group is at the end of the polypeptide chain as this amino acid does not undergo the above tautomeric rearrangement, as the asymmetry of the carbon is not affected.

HYDROLYSIS BY ENZYMES

In the study of the constitution of proteins the hydrolytic cleavage of the protein molecule into amino acids is usually accomplished by boiling with dilute acids. Boiling with alkalis, e.g. barium hydroxide, $\text{Ba}(\text{OH})_2$, also produces hydrolysis. We have also mentioned the fact that enzymes hydrolyze proteins and the two groups of secondary derived proteins, viz., proteoses and peptones, are principally the result of enzymatic hydrolysis. In general it may be said that enzymatic hydrolysis of proteins proceeds more gradually and permits the easier isolation of intermediate products than acid hydrolysis. While the study of enzymatic action belongs more to a study of biological chemistry than to systematic organic, yet it is well here, as in the case of carbohydrates, to mention the enzymes that are especially important.

Proteolytic Enzymes.—The enzymes which hydrolyze proteins are called *proteolytic enzymes* or **proteases**. They belong to the general class of *hydrolytic enzymes*. The more important representatives are those found in the animal body which are involved in the processes of food digestion. The following may be mentioned with the hydrolytic products produced in normal food digestion. **Pepsin**, the proteolytic enzyme present in the gastric juice of the stomach. It hydrolyzes proteins in the most part to proteoses, peptones and peptides. By prolonged action or under artificial conditions pepsin may yield amino acids also. **Trypsin**, the proteolytic enzyme present in the activated pancreatic juice, hydrolyzes proteins *in part* to proteoses, peptones and peptides but *mostly* to amino acids. **Erepsin**, the proteolytic enzyme of the intestinal juice, hydrolyzes protein but *mostly* proteoses, peptones and peptides to amino acids.

QUALITATIVE TESTS

Color Reactions.—Proteins respond to certain empirical qualitative tests made by means of reagents some of which give color reactions and some precipitations. In general all proteins respond to the color tests and in some cases non-protein compounds also. Some of the color reactions have been shown to be due to the presence of certain groups in the protein molecule and they thus indicate a differentiation though this is not sufficient in most cases to be of much value.

Millon's Reaction.—This reaction is produced by a reagent known as **Millon's reagent** which contains a mixture of mercurous nitrate and nitrite in nitric acid. It is made as follows: dissolve one part by weight of mercury in two parts by weight of concentrated nitric acid (sp. gr. 1.42) and then dilute with two volumes of water. The test works best with solid proteins and when to a little of the protein a few drops of Millon's reagent is added and then warmed a yellow or white color changing to red indicates protein. The test is produced by any compound containing the *hydroxy-phenyl group*, ($-\text{C}_6\text{H}_4\text{OH}$). As the amino acid tryosine, $\text{C}_6\text{H}_4(\text{OH})-\text{CH}_2-\text{CH}(\text{NH}_2)-\text{COOH}$, is the only one containing this group the test will be given only by proteins which yield this acid on hydrolysis. Gelatin and some of the protamines do not yield tryosine on hydrolysis and do not respond to Millon's test. On the other hand certain non-nitrogenous compounds like **phenol**, $\text{C}_6\text{H}_5-\text{OH}$,

salicylic acid, $\text{C}_6\text{H}_4 \begin{matrix} \text{OH} \\ \diagup \\ \text{COOH} \end{matrix}$, and **thymol**, $\text{C}_6\text{H}_3 \begin{matrix} \text{CH}_3 \\ \diagup \\ \text{OH} \\ \diagdown \\ \text{CH}(\text{CH}_3)_2 \end{matrix}$,

respond to the test.

Biuret Reaction.—This reaction is produced with solutions of proteins by dilute copper sulphate in presence of strong alkali. To a little protein solution add an equal volume of strong potassium hydroxide and mix. Add to this a few drops of *very dilute* copper sulphate (2 drops 10 per cent CuSO_4 to about 10 cc. water). A pinkish violet color due to the formation of a copper compound indicates protein. The reaction gets its name from the fact that **biuret**, $\text{H}_2\text{N}-\text{CO}-\text{NH}-\text{O}-\text{NH}_2$, formed from urea by the loss of ammonia from two molecules (p. 434), responds to the test. It is due to the presence in the protein and other compounds, of *two amino groups*, ($-\text{NH}_2$), one of which may have substitution groups within it, the two groups being linked to differ-

ent carbon atoms. As this condition is present in any protein or polypeptide all proteins and derived proteins respond. In addition to the proteins, non-protein compounds other than biuret, such as **oxamide**, $\text{H}_2\text{N}-\text{CO}-\text{CO}-\text{NH}_2$, and **asparagine** $\text{H}_2\text{N}-\text{OC}-\text{CH}_2-\text{CH}(\text{NH}_2)$

$-\text{COOH}$ give positive tests. Urea, $\text{CO} \begin{array}{l} \text{NH}_2 \\ \text{NH}_2 \end{array}$, on the other hand

with two amino groups linked to one carbon atom, does not respond to the test.

Xanthoproteic Reaction.—This reaction is produced by the action of concentrated **nitric acid** and results in a yellow color which turns orange on the addition of ammonium hydroxide. The yellow stain of nitric acid on flesh is due to the protein that is present. The reaction is caused by the presence of the *phenyl* group, (C_6H_5-) , and any non-protein compound containing this group also gives the test.

Hopkins-Cole Reaction. Glyoxylic Acid Reaction.—This reaction is produced with proteins by the action of **glyoxylic acid**, $\text{CH}(\text{OH})_2-\text{COOH}$ (p. 252). To a little protein solution add an equal volume of a solution of glyoxylic acid made by reducing oxalic acid with sodium amalgam. Mix thoroughly and then introduce an equal volume of concentrated sulphuric acid by means of a pipette reaching to the bottom of the test tube so as not to mix the acid and the solution. A reddish-violet color at the zone between the two liquids shows the presence of protein.

Precipitation Tests.—Several reagents possess the property of precipitating proteins from solution as *unchanged protein*.

Precipitated Protein.—**Ammonium sulphate**, when added to saturation, precipitates from solution *all proteins* and derived proteins *except peptones*. **Sodium chloride** similarly precipitates *only globulins*, if the solution is neutral, but *all except peptones*, if acid is added.

Metal Albuminates.—Salts of certain metals, e.g., **mercuric chloride**, HgCl_2 , and **lead acetate**, $(\text{CH}_3\text{COO})_2\text{Pb}$, precipitate albumin from solution in the form of insoluble *metal albuminates*. These reactions are the basis for the use of white of egg as an *antidote* for poisoning with mercuric chloride.

Precipitated Meta-proteins.—Mineral acids, nitric, hydrochloric, sulphuric and strong organic acids, like acetic acid, precipitate albumin as *insoluble* primary derived proteins, *meta-proteins*.

Soluble Acid Albuminates.—These meta-proteins are dissolved with excess of acid in the form of *soluble acid albuminates*.

Heller's Ring Test.—The precipitation of albumin with **nitric acid** is the basis for an important clinical test for albumin, especially in urine. 5 c.c. of urine are placed in a test tube, or conical test glass, and an equal volume of strong nitric acid is added at the bottom by means of a pipette. At the zone between the two liquids a *cloud of precipitated albumin* will appear on standing even if a small trace is present.

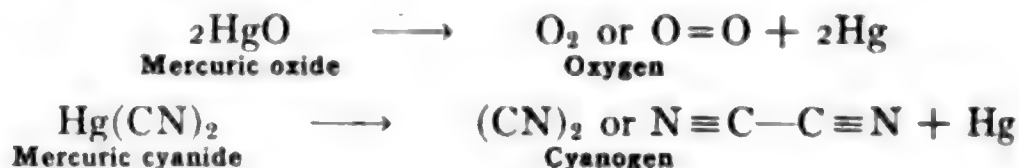
Precipitated Protein Salts.—Other acids, *e.g.*, **picric, phosphotungstic and tannic acids**, precipitate albumins from solution in the form of *insoluble protein salts*. The alkali salts of these acids cause no precipitation. These precipitation tests are used in *salting out* methods for the separation of the proteins, but the limits of differentiation are not sharp and much care is needed to make the separations valuable. More specific details as to methods of manipulation may be found in laboratory texts on physiological chemistry.

XII. CYANOGEN, CYANIDES, CYANATES

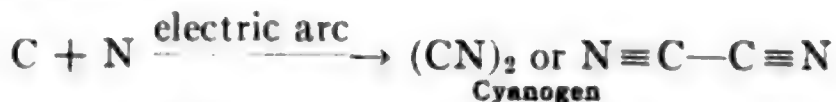
In our discussion of the various groups of compounds we have repeatedly referred to the cyanogen substitution products as analogous to the halogen, hydroxyl and amino compounds, *e.g.* $\text{CH}_3\text{—Cl}$, methyl chloride; $\text{CH}_3\text{—OH}$, methyl (hydroxide) alcohol; $\text{CH}_3\text{—NH}_2$, methyl amine; $\text{CH}_3\text{—CN}$, methyl cyanide. The group (—CN) acts in all respects as a monovalent radical, the compounds being termed *cyanides* or *cyano compounds*.

A. CYANOGEN OR DI-CYANOGEN

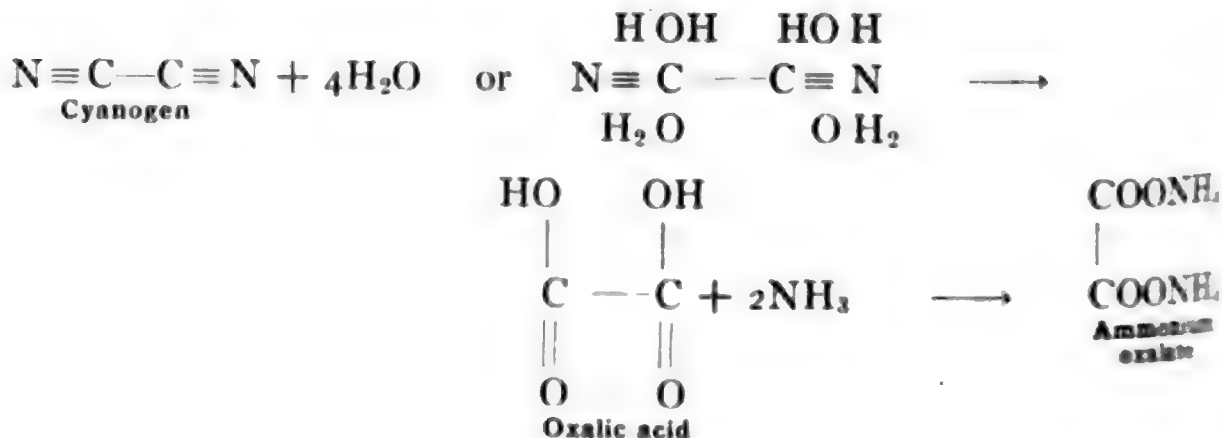
The *cyanide radical* is one of the examples of a radical existing as such. It is known as **cyanogen** and is made by heating mercuric cyanide just as oxygen is made by heating mercuric oxide.



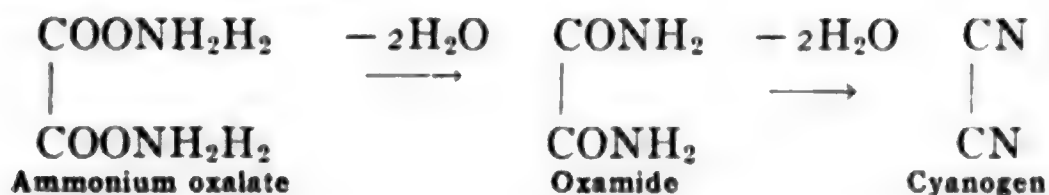
It may also be formed by passing nitrogen over an electric arc between carbon electrodes.



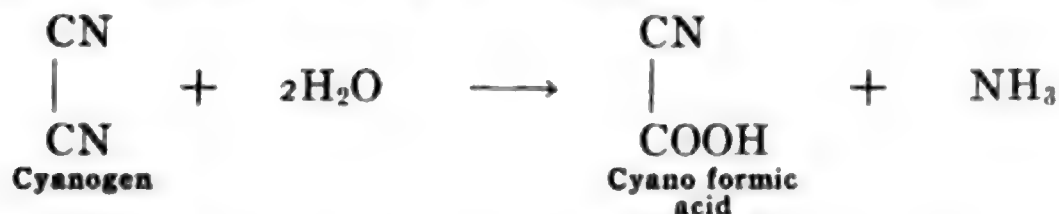
That cyanogen is $\text{N}\equiv\text{C—C}\equiv\text{N}$ is proven both by its analogy to molecular oxygen, in the above formation from mercuric cyanide, and by the fact that it is the *nitrile* of **oxalic acid**. When hydrolyzed it reacts with four molecules of water and yields oxalic acid and ammonia which then, of course, unite and form ammonium oxalate.



The reverse of this reaction also occurs and ammonium oxalate yields cyanogen by the loss of four molecules of water, **oxamide** (p. 272) being the intermediate product.



This is exactly analogous to the relation between **ammonium acetate**, **acetamide** and **acetic nitrile** or **methyl cyanide** (p. 148). As cyanogen is a *di*-cyanide or a *di*-nitrile we would expect an intermediate product formed by the hydrolysis of *only one* nitrile group. Such a compound would be **cyano formic acid** and a *semi-nitrile* of oxalic acid.



The compound is not known free but in the form of its esters.

Cyanogen is a stable colorless gas with a sharp odor. It is easily condensed to a colorless liquid boiling at -20.7° and solidifies, when cooled below this temperature, to crystals which melt at -34.4° . Gaseous cyanogen burns with a blue flame and is decomposed only at high temperatures (above 800°). It is soluble in water but the water solution is unstable, decomposing into **oxalic acid**, **ammonia**, **carbon dioxide**, **hydrogen cyanide** and **urea**. With alkalis cyanogen yields **cyanides** and **cyanates**.



This is analogous to the reaction of chlorine and alkalies.

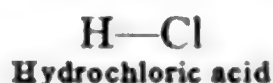
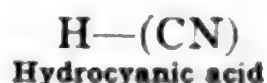


B. HYDROCYANIC ACID AND ITS SALTS

Hydrocyanic Acid H—CN Hydrogen Cyanide

Hydrocyanic acid or **hydrogen cyanide** is the simple binary acid of cyanogen, corresponding to hydrochloric acid, the binary acid of chlorine.

The group (CN) is considered as a unit and is sometimes denoted by the symbol Cy, but this is not desirable.



Hydrocyanic acid is most easily prepared from its potassium salt, $\text{K}(\text{CN})$, which is obtained principally by the decomposition of the complex double cyanides of iron as we shall soon consider. The acid is also obtained by the hydrolysis of certain glucosides, *e.g.*, **amygdalin**, in bitter almonds. It is prepared synthetically by reactions to be discussed presently in connection with the constitution of it and its salts. It is a colorless liquid with a characteristic odor and burns with a violet flame. It boils at 26.1° and solidifies to crystals which melt at -14° . It is an *extremely strong poison*, the best antidotes being chlorine and hydrogen dioxide. It is readily absorbed by metallic nickel which is thus used in gas masks for this purpose. It is stable in dry air but in presence of water is readily hydrolyzed yielding **ammonia** and **formic acid** as the chief products.



Formic Nitrile.—It is thus known also as **formic nitrile**.

Metal Cyanides

The two simple salts of hydrocyanic acid which are used in the synthesis of organic cyanogen compounds are **potassium cyanide**, $\text{K}-(\text{CN})$, and **silver cyanide**, $\text{Ag}-(\text{CN})$. These are both prepared by the action of the metallic oxides or hydroxides on the acid.

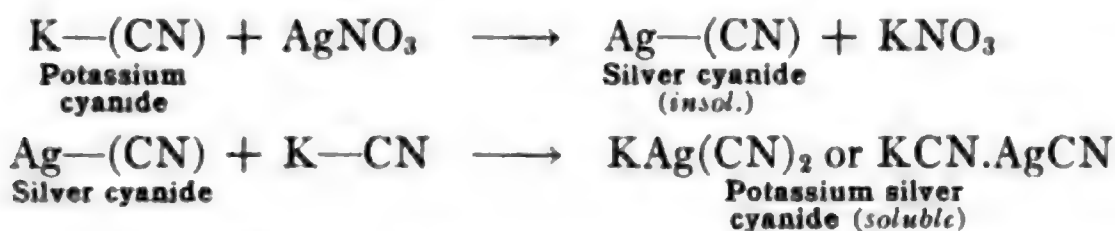


The silver cyanide is also formed by the reaction between potassium cyanide and silver nitrate.



Potassium cyanide is a white deliquescent solid readily soluble in water. It is easily decomposed by boiling the water solution and yields potassium formate and ammonia. Like hydrocyanic acid it is an *extremely violent poison*, probably due to its hydrolysis into the free acid. It also yields hydrocyanic acid by the action of carbonic acid. It is prepared commercially by the decomposition of the double cyanide of iron and potassium, **potassium ferro-cyanide**, $K_4Fe(CN)_6$. In recent years it has been used extensively as a solvent for gold in the recovery of this metal from low-yielding ores.

Silver cyanide is a white solid readily formed as a precipitate when solutions of silver are treated with potassium cyanide. It is readily soluble in excess of potassium cyanide forming the double cyanide of silver and potassium. It is also soluble in ammonium hydroxide.



Constitution.—The problem of the constitution of hydrocyanic acid and its simple salts potassium cyanide and silver cyanide is a very interesting one though the facts bearing upon it are very puzzling. In considering the cyanogen substitution products of the hydrocarbons we showed by very satisfactory evidence that they existed in two distinct isomeric forms, viz., **alkyl cyanides**, $R-C \equiv N$ and **alkyl isocyanides** $R-N \equiv C$ or $R-N=C$. The proofs for this view are furnished by the hydrolytic decomposition of the two compounds (p. 69). The products obtained show conclusively that in the *cyanides* the *alkyl carbon atom is linked to the carbon atom* of the cyanogen radical, while in the *iso-cyanides*, the *alkyl carbon atom is linked to the nitrogen atom* of the cyanogen.



Now while isomerism exists in the alkyl cyanogen compounds there is *no* isomerism in the case of either hydrocyanic acid, potassium cyanide or silver cyanide. Each of these compounds is known in *only one form*.

It would seem therefore that the only problem would be to determine whether they exist in the form of alkyl cyanides, *i.e.*, with the hydrogen, potassium or silver linked to the carbon atom of the cyanogen or whether they are in the form of the alkyl isocyanides with the nitrogen atom of the cyanogen group linked to the other element. This, however, is where the facts become perplexing.

Synthesis from Cyanogen.—Two methods of synthesis of hydrocyanic acid support the view that this compound *has the cyanide structure* and not the iso-cyanide. Cyanogen gas because it yields oxalic acid on hydrolysis must have the constitution in which the two cyanogen groups are linked by the carbon atoms rather than nitrogen.



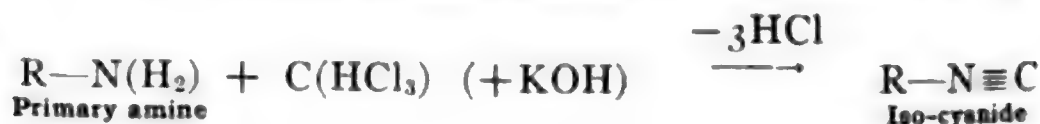
Now cyanogen yields hydrocyanic acid when acted upon by hydrogen under the influence of a silent electrical discharge. The only way for hydrogen to split the cyanogen molecule and form hydrocyanic acid would be at the union between the two carbon atoms. The hydrogen itself thus becoming linked to carbon



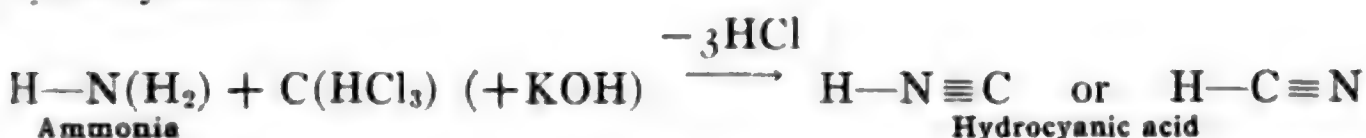
From Acetylene.—The second synthesis of hydrocyanic acid supporting this same constitution is from **acetylene** by reaction with nitrogen under the influence of an electrical discharge. The nitrogen would split the acetylene molecule at the triple linkage of the two carbons leaving each hydrogen linked to carbon in the hydrocyanic acid.



From Ammonia.—A third method for the synthesis of hydrocyanic acid supports the constitution of an *iso-cyanide* with the linkage of hydrogen to nitrogen. The **Hofmann iso-nitrile reaction** (p. 71) consists in the formation of iso-cyanides (iso-nitriles) by the reaction between chloroform and primary amines in the presence of an alkali



Now if instead of a primary amine we use ammonia the product is hydrocyanic acid.



Alkyl Cyanides from Potassium Cyanide.—That potassium cyanide has the constitution corresponding to an alkyl cyanide is supported by the fact that alkyl halides with potassium cyanide yield alkyl cyanides and not isocyanides.



Alkyl Iso-cyanides from Silver Cyanide.—On the other hand **silver cyanide** would seem to have the constitution of an *iso-cyanide* because it yields alkyl iso-cyanides with alkyl halides.



While these reactions support *one constitution for potassium cyanide and the other for silver cyanide* yet the two compounds are each prepared from hydrocyanic acid by the action of the respective metallic hydroxides.

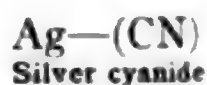
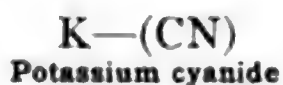
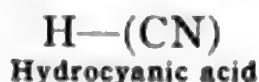


Also, which is still more perplexing, the potassium cyanide, which seems to have the constitution of a cyanide when it reacts with silver nitrate yields silver cyanide which, as above, seems to have the constitution of an isocyanide.



Tautomerism.—While therefore these three cyanogen compounds do not exist in isomeric forms as do the alkyl cyanogen compounds yet we cannot assign one definite formula to each compound because the evidence goes to show that *sometimes one formula and sometimes the other is the true representation of the constitution*. The two forms probably exist together in equilibrium the conditions of which are different for each of the compounds so that though they are very similar in character their apparent constitution is different. Thus we have another inter-

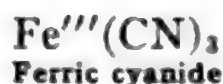
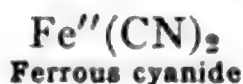
esting case of the peculiar phenomenon of *tautomerism* as was found especially in the case of aceto-acetic ester (p. 256). In writing the formulas therefore it is best not to indicate a definite constitution but simply the linkage of the cyanogen group as a whole with the other elements.



Complex Iron-cyanide Compounds

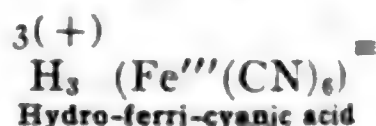
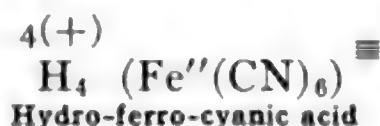
Aside from potassium cyanide in its use for the extraction of gold the most important cyanides commercially are the double cyanides of iron and potassium.

Ferrous and Ferric Cyanides.—Iron being both *bivalent* and *trivalent* forms two salts with hydrocyanic acid

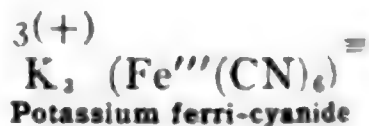
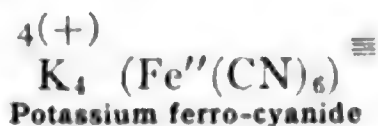


These two simple salts are not known; but with hydrocyanic acid, with potassium cyanide, with themselves or with each other, they form well known *double cyanides*. These double cyanides, however, are really simple compounds which dissociate, in solution, into two *ions*, viz., the *cation*, of hydrogen or the metal, and a complex *anion*, consisting of iron and the cyanogen group.

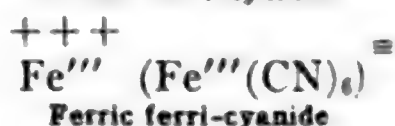
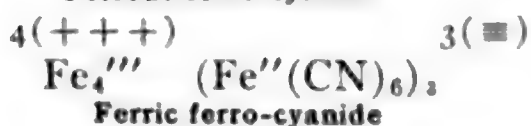
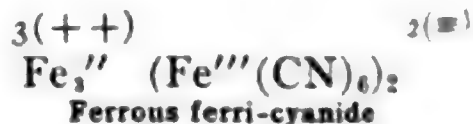
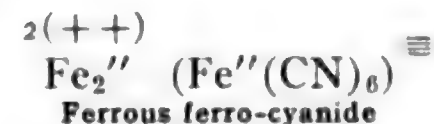
Hydro-ferrocyanic and Hydro-ferricyanic Acids.—The acids which are the mother substances of these complex cyanides may be obtained from the potassium salts by treating with strong acids. They are:



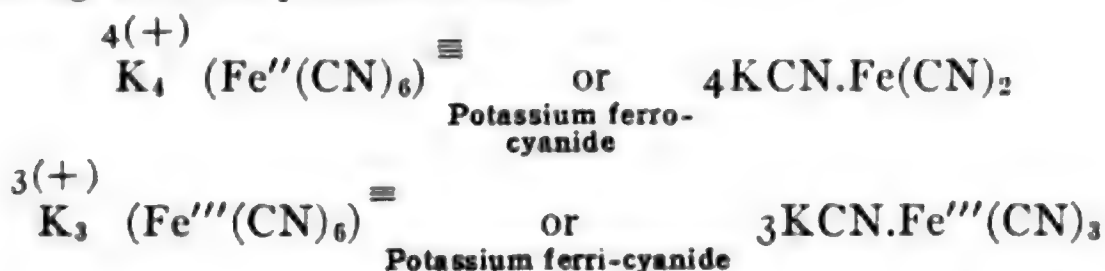
Potassium Salts.—These two acids form salts with potassium as follows:



Iron Salts.—They also form salts with iron both as *ous* salts and *ic* salts.



In all of these ferro- and ferri-cyanides we have the complex *anions* $(\text{Fe}''(\text{CN})_6)$, = **ferro-cyanide**, and $(\text{Fe}'''(\text{CN})_6)$, = **ferri-cyanide**. The **ferro-cyanide ion** possesses *four negative charges* and the iron is in the *ous* condition; while the **ferri-cyanide ion** possesses *three negative charges* and the iron is in the *ic* condition. In order to indicate their double salt composition these formulas are sometimes written as follows, illustrating with the potassium salts.



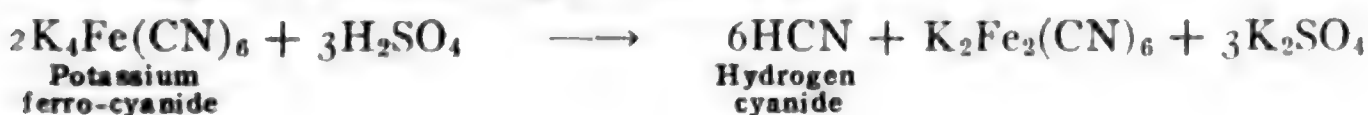
While these formulas express the double salt composition they do not indicate how the compounds dissociate in solution and how solutions of them react.

The iron salts of ferro and ferricyanic acid are the compounds to which the names cyanogen and cyanide are due. Two of these salts are of deep *blue* color and the Greek word from which cyanogen and cyanide are derived is *cyanos* which means *blue*. The **ferric ferro-cyanide**, $\text{Fe}_4'''(\text{Fe}''(\text{CN})_6)_3$, is known as **Prussian blue** and the **ferrous ferri-cyanide**, $\text{Fe}_3''(\text{Fe}'''(\text{CN})_6)_2$, is **Turnbull's blue**. These compounds are formed when ferric salts in solution are treated with potassium ferro-cyanide and when ferrous salts in solution are treated with potassium ferricyanide. They are common qualitative tests for the two forms of iron salts. The compounds are also used as laundry blueing and are formed in the blue print process of photography.

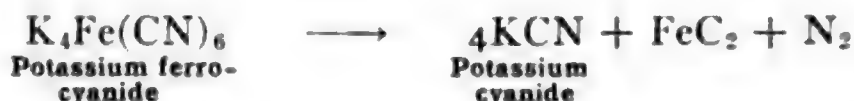
Potassium Ferro-cyanide.—Potassium ferro-cyanide is commercially prepared by heating nitrogenous organic material, *i.e.*, **protein** (blood, hair, horn, leather, etc.) with **potassium carbonate** and **iron filings**. The mixture is heated red hot, after cooling is extracted with water and the potassium ferro-cyanide crystallized out.



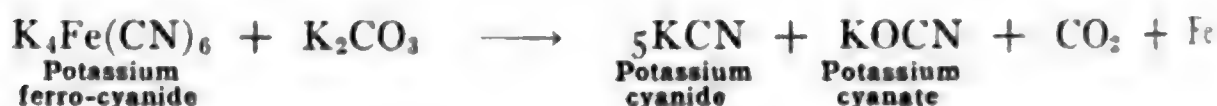
Potassium ferro-cyanide so prepared is the starting point for the preparation of the other cyanogen compounds. When distilled with *dilute sulphuric acid*, **hydrogen cyanide** is evolved.



When *heated alone* it decomposes yielding **potassium cyanide**, **iron carbide** and **nitrogen**.



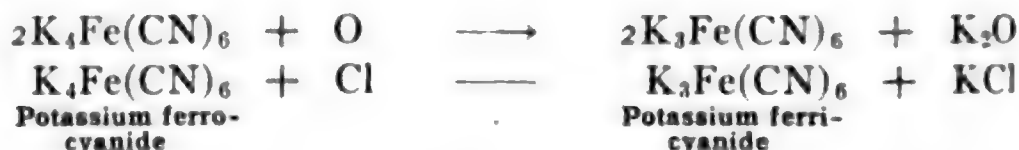
When similarly *heated with potassium carbonate* a larger yield of potassium cyanide is obtained.



Heated with metallic sodium all of the cyanogen is obtained as cyanide.



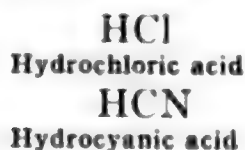
On *oxidation* of the ferro-cyanide by means of potassium permanganate, potassium bichromate, bromine or chlorine, the **ferri-cyanide** is obtained.



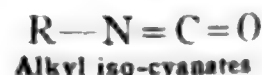
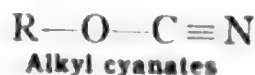
C. CYANIC ACID, ISO-CYANIC ACID, THIO-CYANIC ACID AND THEIR SALTS

Cyanic and Iso-cyanic Acids and Salts

Iso-cyanic Acid.—If hydrocyanic acid is analogous to hydrochloric acid we should expect an oxygen acid to be obtained from it analogous to hypochlorous acid.

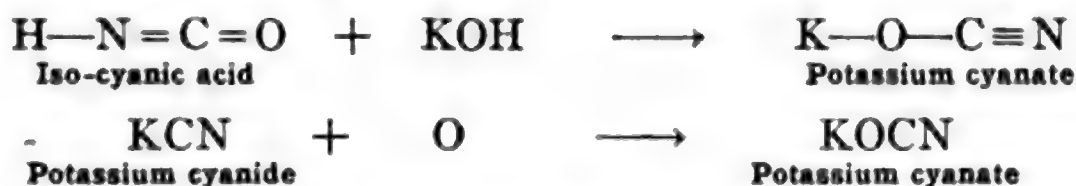


An acid of this composition is known but it has been shown to have another constitution, viz., $\text{H}-\text{N}=\text{C}=\text{O}$, and is **iso-cyanic acid** though it is often called cyanic acid. It is an odorous, unstable liquid. We have already discussed (p. 73) the alkyl derivatives of these two acids.

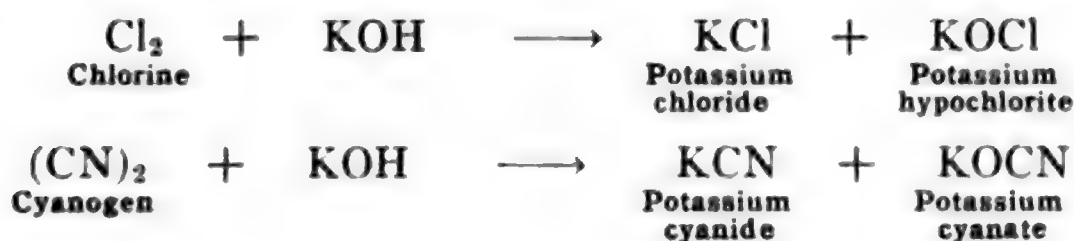


Thus while isomeric derivatives are known corresponding to two isomeric acids only one acid is known and this one has the structure of the **iso-cyanic acid**. When we study the salts obtained from this iso-cyanic acid we find, unlike the alkyl derivatives, that they are known in only *one* form but strangely enough in the form of the **cyanic acid**, e.g., $\text{K—O—C}\equiv\text{N}$, **potassium cyanate**.

Potassium Cyanate.—When **iso-cyanic acid** is neutralized with potassium hydroxide, potassium cyanate is obtained. **Potassium cyanate** is also obtained when **potassium cyanide** is oxidized by means of lead oxide or potassium bichromate.



The preparation of this compound by this reaction is an exceedingly striking one. It is usually accomplished by heating anhydrous **potassium ferro-cyanide** with dry potassium bichromate in an iron dish. The ferro-cyanide is first decomposed by the heat as previously described (p. 416) yielding five molecules of potassium cyanide and one molecule of potassium cyanate. The potassium cyanide is then oxidized by the bichromate to potassium cyanate. A little of the mixed ferro-cyanide and bichromate is placed in the center of a hot iron dish. The mass soon glows and becomes red hot at the same time turning black due to the setting free of the iron. A tinge of green is also often observed indicating reduction of the bichromate. The outside heat may now be removed and as fresh mixture is added, in small quantities at a time, the reaction continues until a black mound is formed which is red hot all through. This is then cooled, extracted with hot alcohol and filtered into a cold dish when the potassium cyanate separates out in fine crystals. Potassium cyanate bears the same relation to potassium cyanide that potassium hypochlorite bears to potassium chloride. They are respectively formed when chlorine gas or cyanogen gas is passed into potassium hydroxide.

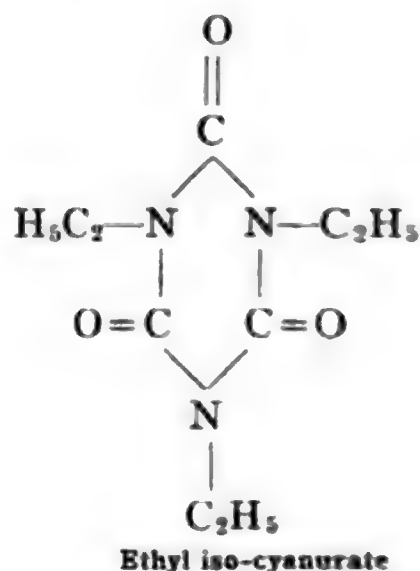
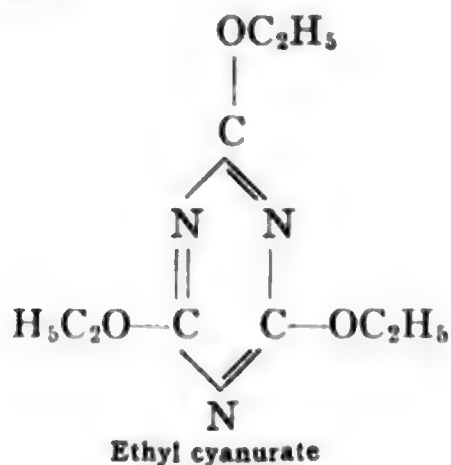


Ammonium Cyanate.—The corresponding ammonium salt, viz., **ammonium cyanate**, NH_4OCN , may be easily prepared from the potassium cyanate by treating a solution of the latter with the calculated amount of ammonium sulphate. This compound is of especial interest because on evaporation of the water solution to dryness a rearrangement takes place and **urea** is formed (p. 429). Ammonium cyanate is also formed when iso-cyanic acid is neutralized with ammonia.



Such a rearrangement when iso-cyanic acid is neutralized and converted into salts of cyanic acid is an interesting phenomenon.

Cyanuric Acid.—That iso-cyanic acid has the constitution given to it is established by the constitution of the alkyl derivatives which are not true esters (p. 73) and also by its relation to **cyanuric acid**. This latter acid is a *polymer* of iso-cyanic acid, viz., $(\text{HNCO})_3$. It is obtained by heating **urea** and the reactions will be considered presently when we study this compound. This source of the acid is the basis of the name **cyan-uric acid**. It is a solid crystallizing from water solution in prisms which contain two molecules of water of crystallization. Like iso-cyanic acid cyanuric acid yields alkyl derivatives of two isomeric forms, corresponding to polymers of cyanic and iso-cyanic acid derivatives. The ethyl derivatives have the following constitutions:

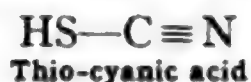
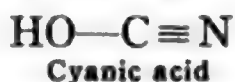
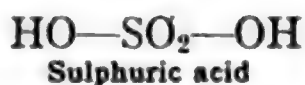


In all of these cyanogen compounds we have this striking phenomenon of the probable existence of *tautomeric forms in equilibrium*. In some cases, as in the acids and the metal salts, the conditions of equi-

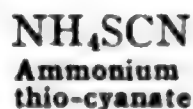
handled in the moist condition. The fulminate detonating caps may be exploded by percussion as in the case of gun cartridges or by means of heat produced by a burning fuse or by an electric spark as in the case of shells and dynamite cartridges.

Thio-cyanic Acid and Salts

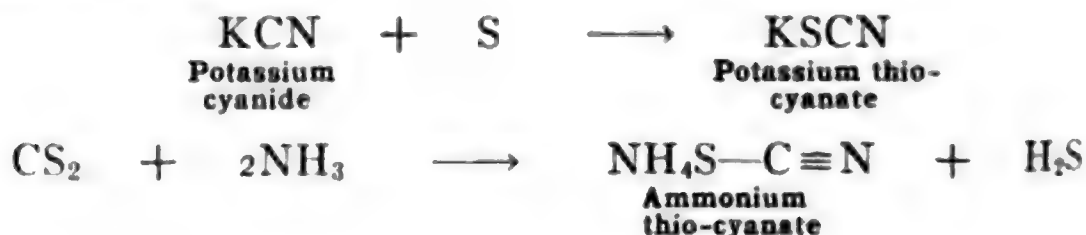
Corresponding to the cyanic and iso-cyanic acids and their salts and esters, we have the analogous **sulphur** or **thio** compounds formed by the replacement of oxygen by sulphur. The relationship of these sulphur compounds to the oxygen compounds is exactly the same as that existing between **sulphuric acid** and **thio-sulphuric acid**.



While free cyanic acid is not known the thio-cyanic acid is a more or less stable liquid. The salts of thio-cyanic acid are also known, two of them being quite common reagents, viz.,



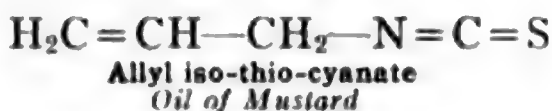
With ferric salts in solution either of these reagents forms the cherry red **ferric thio-cyanate** and is the basis of qualitative tests for iron and the use of the thio-cyanate as an indicator in volumetric titrations. Potassium thio-cyanate may be prepared by heating potassium cyanide with sulphur or ammonium sulphide. **Ammonium thio-cyanate** may be prepared by heating together carbon disulphide and ammonia in the presence of alcohol.



This compound undergoes rearrangement the same as ammonium cyanate and **thio-urea** is obtained. With a soluble mercuric salt ammonium thiocyanate precipitates **mercuric thio-cyanate** which on heating swells up into phantastic shapes which are known as **Pharaoh's serpents**. The alkyl thio-cyanates are known and have been discussed (p. 74). **Allyl-thio-cyanate** is a constituent of oil of garlic. These

compounds are true sulphur esters agreeing with the constitution of thio-cyanic acid as HSCN .

Iso-thio-cyanates.—Isomeric with the thio-cyanic acid would be **iso-thio-cyanic acid** which if analogous in constitution to the iso-cyanic acid should have the constitution H—N=C=S . Neither this compound nor metal salts of it are known but alkyl derivatives are known as constituents of oil of mustard (p. 165).



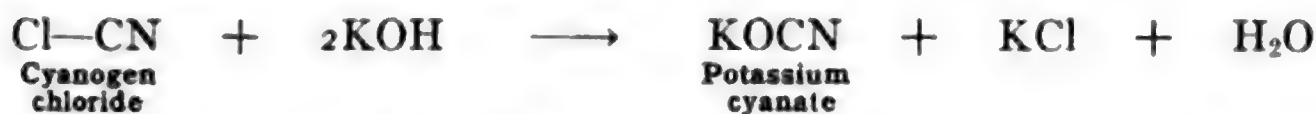
These iso compounds are obtained from the thio-cyanates by heat and their constitution is analogous to that of the alkyl iso-cyanates. They are not true sulphur esters but the alkyl radical is linked to nitrogen as is proven by their hydrolysis to primary amines.

Cyanogen Chloride and Cyan-amide

Cyanogen Chloride.—This compound is the simple chlorine compound of cyanogen and is formed by the action of chlorine on hydrocyanic acid.



It is a soluble colorless gas with a strong odor and is used in synthesizing cyanogen compounds.



Cyanamide.—An important compound formed from cyanogen chloride is known as **cyan-amide** and as its name indicates is composed of the *cyanogen radical* linked to the *amine radical*. It may be formed by the action of **ammonia**, in ethereal solution, on **cyanogen chloride**.



It is a white crystalline substance slightly soluble in water. This compound is of especial interest because it acts *both* as a *weak base* and as a *weak acid*. The metallic salts are the more stable and the most important one is the calcium salt.

Calcium Cyanamide.—Calcium cyan-amide may be formed from the cyanamide itself by the action of lime.



This synthesis, however, is not the most important nor the most interesting.

Fixation of Atmospheric Nitrogen.—The great value of this cyanogen compound lies in the two facts; (1) that it may be obtained as the result of the *fixation of atmospheric nitrogen* and (2) that it is a valuable *nitrogen fertilizer*.

In 1895–1898 **Caro** and **Frank** and others endeavored to synthesize cyanide compounds by the action of atmospheric nitrogen on **barium carbide** at about 700°C. They obtained only small yields of the simple **barium cyanide**, but much larger of **barium cyan-amide**. In utilizing **calcium carbide**, instead of barium carbide, a yield of about 90 per cent. of the **cyan-amide** was obtained at 1000°C. The preparation of the calcium carbide and the fixation of the atmospheric nitrogen was carried out in the same operation by heating together **quick lime**, **CaO**, **carbon** and atmospheric **nitrogen** in an electric furnace.



The atmospheric nitrogen must be free of oxygen, which is usually accomplished by passing the air over heated copper, or by utilizing nitrogen obtained from *liquid air*. The calcium cyanamide obtained contains about 20 per cent. *nitrogen*.

A Source of Cyanides and Ammonia.—It may be used for making potassium or sodium cyanides by fusing with potassium hydroxide or sodium hydroxide. It may also yield ammonia by the action of steam and carbon dioxide, the reaction being the same as in the hydrolysis below.

Fertilizer.—The chief interest in the compound is, however, in its use as a *nitrogen fertilizer*, for which purpose about 50,000 tons are made annually, at the present time, in the United States. The manufacture in this country began about 1909. As a fertilizer it may be used either directly or indirectly. The indirect use is as a source of ammonia, by the method just referred to. The ammonia so obtained is then converted into salts which are the actual constituents of the

fertilizers. A special product so made is known as *ammo-phos* and contains both **ammonia-nitrogen** and **phosphoric acid**. The direct use is as a constituent of mixed fertilizers, in which case it is usually one of several nitrogen compounds present. It is claimed that, in general, the crude calcium cyanamide yields its nitrogen to crops equally with ammonium sulphate and equal to 90 per cent of that in sodium nitrate. The hydrolysis of the compound may be represented by the following reaction.



The decomposition in the soil is however influenced by varying conditions and by the presence of lime and other fertilizer salts so that its exact value is yet in question. Among the products obtained by its decomposition in the soil are; **ammonia** NH_3 , **calcium carbonate**, CaCO_3 , **cyan-amide**, $\text{H}_2\text{N}-\text{CN}$, **di-cyan di-amide**, $(\text{H}_2\text{NCN})_2$ or $\text{H}_2\text{N}-(\text{HN})\text{C}-\text{NH}(\text{CN})$, **cyano guanidine** and **urea** $\text{OC}(\text{NH}_2)_2$. Further discussion of its use as a fertilizer is not desirable here.

Sodium Cyanide from Atmospheric Nitrogen.—One other method for the fixation of atmospheric nitrogen in the form of cyanide compounds should be mentioned before we leave the subject of cyanogen compounds. This is the recent American process of **Bucher** in 1917. It consists in fixing the nitrogen of the atmosphere in the form of **sodium cyanide**, NaCN . Such a fixation of nitrogen as a metal cyanide had been accomplished by **Thompson** as early as 1839 by heating together **potassium carbonate**, K_2CO_3 , **carbon**, C , and atmospheric **nitrogen** gas in the presence of **iron**. The process as originally carried out proved not to be successful and up to 1917 no successful process for converting atmospheric nitrogen into metal cyanides was in operation. **Bucher** recognized the important rôle of metallic iron as a catalytic agent and developed **Thompson's** method, fixing the nitrogen of the air according to the following reaction including the energy factor.



The energy required, represented by 138,500 cal., is counterbalanced by the energy obtained in burning the carbon monoxide produced, which amounts to +200,000 cal., so that the total energy reaction is an *exothermic* one. The result was obtained by using either air, pure

nitrogen gas or producer gas. At the present time the process is being perfected industrially and bids fair to be another successful method of fixing the nitrogen of the atmosphere. Further details may be found in the original articles in Jour. Ind. & Eng. Chem., 9, 233 (1917). The process is valuable not only in producing sodium cyanide, which has a certain value of its own, but from the fact that from the cyanide other products are able to be obtained. Some of the possible products are the following, all of which have important uses in the industries or as fertilizers. **Sodium ferrocyanide**, $\text{Na}_4\text{Fe}(\text{CN})_6$, **sodium hydroxide**, NaOH , **ammonia** NH_3 from which nitric acid, HNO_3 , may be obtained by oxidation, **sodium formate**, $\text{H}-\text{COONa}$, **sodium**, Na , **cyanogen**, $(\text{CN})_2$, **oxamide**, $\text{H}_2\text{N}-\text{OC}-\text{CO}-\text{NH}_2$, **oxalic acid**, $\text{HOOC}-\text{COOH}$, **sodium cyanate**, NaOCN , **ammonium cyanate**, NH_4OCN , and **urea**, $\text{OC}(\text{NH}_2)_2$. The reactions involved in these transformations have all been considered previously in this chapter or will be discussed in the following chapter in connection with urea.

XIII. CARBONIC ACID, UREA, URIC ACID, PURINE BASES, ETC.

A. CARBONIC ACID AND DERIVATIVES

CARBONIC ACID

It may appear strange at the outset that the two compounds **carbonic acid** and **urea** should be considered together. Carbonic acid we have always looked upon as *inorganic*, while urea, which is the product of living animals, seems purely *organic*. The fact that these two compounds are very definitely related emphasizes the statement made at the beginning that the characterization of a compound as inorganic or organic rests upon facts of constitution and relationship and not upon those of natural occurrence. It also shows that the line of demarcation between these two large classes of compounds is an indefinite thing for the same compound may rationally be considered as belonging to both.

Carbonates.—Our acquaintance with carbonic acid as an inorganic compound has been through the salts which it forms with the metals and which in general are found abundantly in the earth's crust, *e.g.*, **sodium carbonate**, Na_2CO_3 ; **calcium carbonate**, CaCO_3 , **silver carbonate**, Ag_2CO_3 , etc.

Carbonic Acid.—These salts are derived from the acid which we term **carbonic acid** and to which the formula H_2CO_3 has been assigned. It has never been isolated but is considered to be the product of the reaction between the oxide of carbon, **carbon dioxide**, CO_2 , and water just as sulphuric, nitric and phosphoric acids are the products of the reaction between water and the oxides of sulphur, nitrogen and phosphorus.

Carbon Dioxide.—The fact that carbon dioxide contains the element carbon and that it is the result of the oxidation of the constituents of living animals or plants and also of the oxidation of hydrocarbons such as methane (p. 5) may be considered as the basis for the possible classification of it as an organic compound. This, however, is not the sole reason nor even the more important reason for the classification of carbonic acid as an organic compound.

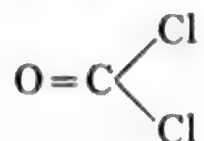
Constitution.—When we attempt to establish the constitution of carbonic acid we shall find additional facts which show that in its

relationship it belongs with the organic compounds though it is not so directly a derivative of the hydrocarbons as some other organic compounds such as alcohols, acids, etc.

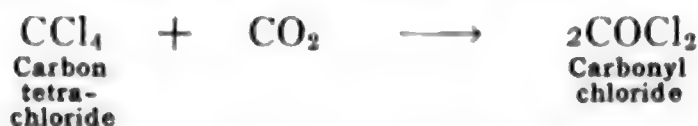
Carbonyl Chloride.—The simplest proof of the constitution of the hypothetical substance carbonic acid, H_2CO_3 , is through the synthesis of its salts and esters from **carbonyl chloride** or **phosgene**, COCl_2 . This latter compound is the product of the reaction of the lower oxide of carbon, viz., **carbon monoxide**, CO , with **chlorine** in the sunlight or in the presence of a carbon catalyser.



Whether we consider, in this reaction, that the *bivalent* carbon of carbon monoxide is changed by the addition of two chlorine atoms to *tetravalent* carbon of carbonyl chloride, or that carbon monoxide is an *unsaturated* compound of tetravalent carbon which by addition of two chlorine atoms forms the *saturated* compound carbonyl chloride, or that in carbon monoxide *oxygen is tetravalent* and becomes *bivalent* in carbonyl chloride, whichever view is held, it is undoubtedly the fact that in **carbonyl chloride** the carbon is *tetravalent* and the constitution is



This constitution of carbonyl chloride is upheld by other syntheses as follows: When **carbon tetrachloride** and carbon dioxide are passed over pumice stone heated to 400° carbonyl chloride is obtained.



Also when carbon tetrachloride is heated with sulphur trioxide or with phosphorus pentoxide to 200° it yields carbonyl chloride by the replacement of two chlorine atoms by oxygen in one molecule of the tetrachloride and all of the chlorine atoms by oxygen in the other molecule, yielding carbon dioxide also.



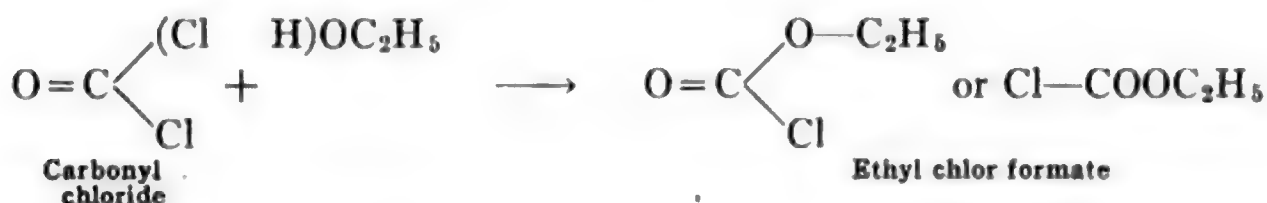
If different proportions are used no carbonyl chloride is obtained but all of the chlorine of carbon tetrachloride is replaced by oxygen and carbon dioxide alone results.



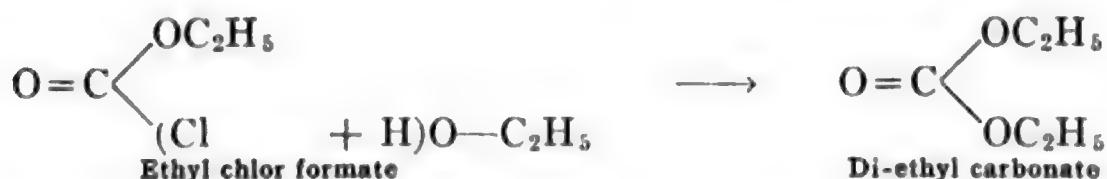
Also **chloroform** when oxidized with potassium bichromate yields carbonyl chloride and chlorine.



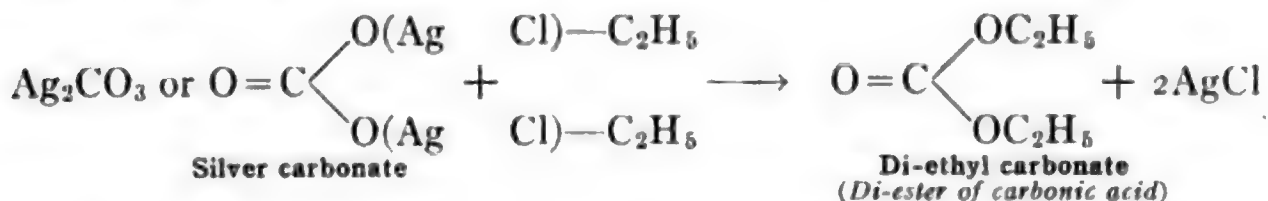
Now when **carbonyl chloride** is passed into **ethyl alcohol** an *ethoxy group* replaces one chlorine atom as follows:



Ethyl Chlor Formate.—The compound formed is an **ethyl ester of chlor formic acid**, and indicates that carbonyl chloride is the **acid chloride of chlor formic acid**. By further action of sodium alcoholate, however, the second chlorine atom is replaced by the ethoxy group.

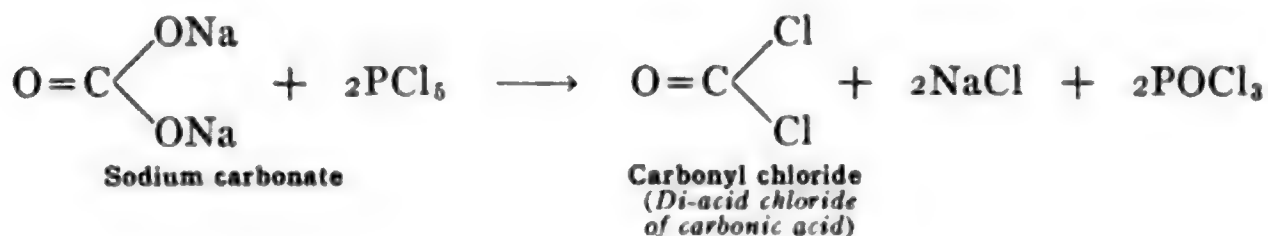


Di-ethyl Carbonate.—This product is a *di-ethyl ester* of carbonic acid, as is proven by the fact that it is also obtained when **silver carbonate**, Ag_2CO_3 , reacts with two molecules of ethyl iodide or chloride.

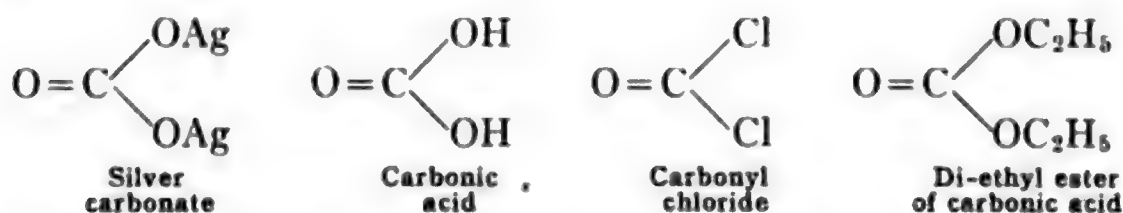


These reactions prove that **carbonyl chloride**, as the name indicates, is the *di-acid chloride* of **carbonic acid**. This is also proven by the fact

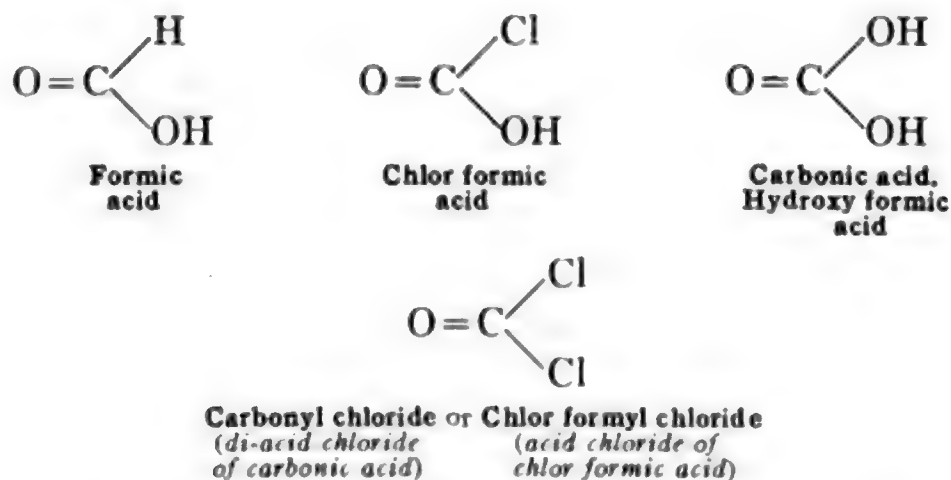
that sodium carbonate with phosphorus pentachloride yields the acid chloride.



These reactions prove that **silver carbonate** must have the constitution given to it above; that the acid from which it is derived, the unisolated **carbonic acid**, has the corresponding constitution; that the di-ethyl compound, formed from carbonyl chloride, is a *di-ethyl ester* of carbonic acid; and **carbonyl chloride** is the *di-acid chloride* of carbonic acid, as follows:

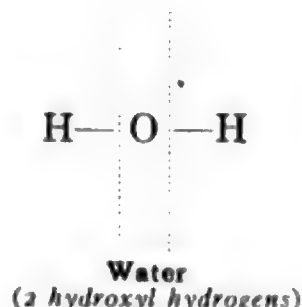
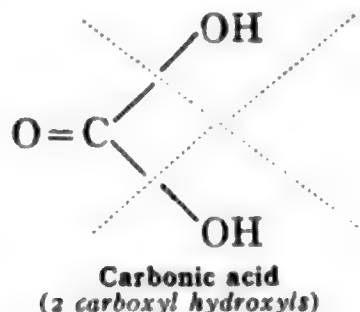


We see, therefore, that carbonyl chloride may be considered as either the *mono-acid chloride* of **chlor formic acid** or the *di-acid chloride* of **carbonic acid**, which means that carbonic acid may also be considered as **hydroxy formic acid**. The following formulas show this relationship



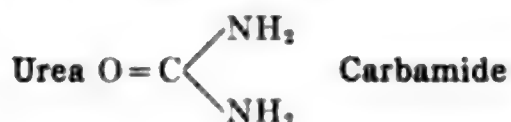
Thus while carbonic acid itself, having never been isolated, is still a hypothetical substance, we know, beyond all doubt, the constitution of its salts, esters and acid chlorides; so that the constitution of the un-

known compound is likewise established. The constitution agrees with the fact that carbonic acid is a dibasic acid. As an organic acid it contains a carboxyl group and, though it does not contain *two* such groups, it contains two hydrogens *both of which* are in *hydroxyl* combination as part of a carboxyl group. This is analogous to water which, though it contains really only one hydroxyl, yet both hydrogens exist in hydroxyl combination.



Phosgene.—One more fact in connection with carbonyl chloride. This compound, known also as **phosgene gas**, is a volatile liquid boiling at 8° . It is one of the **war gases** used in the recent war. It is a vile smelling poisonous substance and was used in shells and bombs, also as a drift gas.

B. UREA AND DERIVATIVES

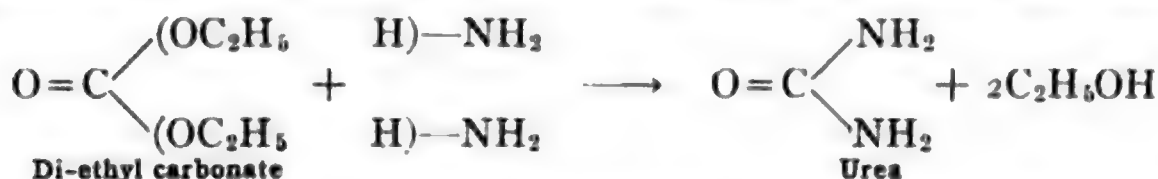


Urea, the principal constituent of animal urine, is important not only physiologically, but also historically. Until 1828 the compound was known only as the product of animal life. In this year **Wöhler** synthesized it from an ordinarily considered inorganic substance which could be made from the elements. This substance was **ammonium cyanate**, and **Wöhler** found that by simply evaporating a solution of it a complete transformation into **urea** was effected. The composition formulas of the two compounds are the same, viz., CH_4ON_2 , *i.e.*, they are isomeric. The synthesis of **Wöhler** shows nothing in regard to the relationship of the two compounds as to structure. It was of extreme importance because it was the *first* instance of a purely organic substance being prepared from elemental or inorganic materials.

Carbamide.—The constitution of urea is shown by its synthesis from **carbonyl chloride** and **ammonia**.



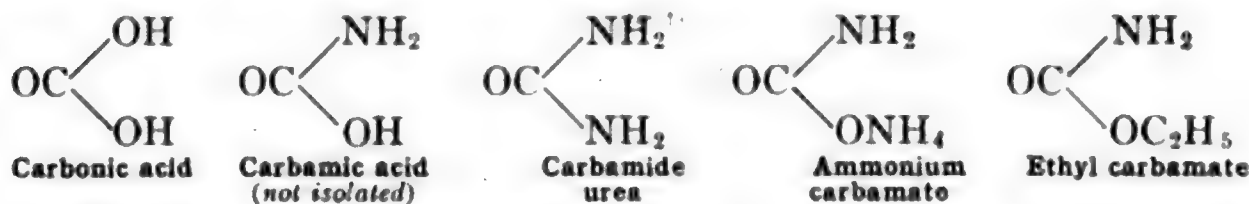
Urea is thus the *di-amide* of carbonic acid and is also termed **carbamide**. It corresponds to carbonyl chloride, the di-acid chloride of carbonic acid. The same constitution is proven in a similar manner by the synthesis of urea from **di-ethyl carbonate** by the action of **ammonia**.



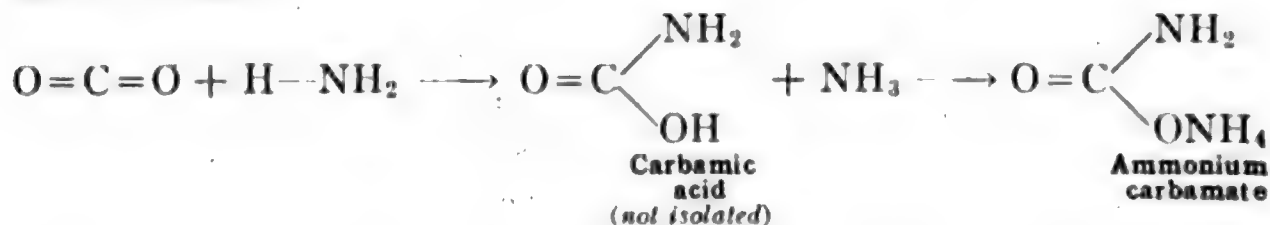
Carbamic Acid.—It will be recalled that oxalic acid, the simplest dicarboxylic acid, yields a corresponding di-amide and that there is also formed an intermediate product known as oxamic acid.



A similar compound, viz., **carbamic acid**, stands intermediate between carbonic acid and carbamide (urea). It is not known, however, as such but as the ammonium salt or as an ester.

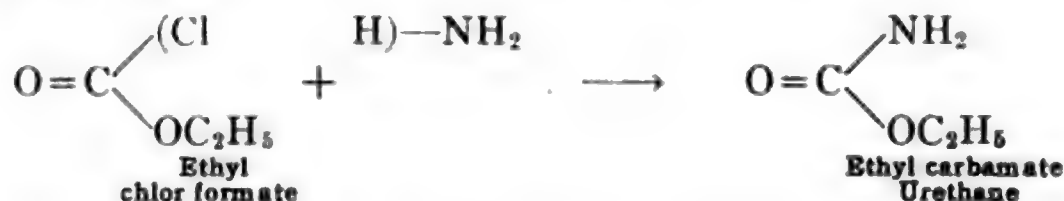


Ammonium carbamate is made by the action of ammonia and carbon dioxide

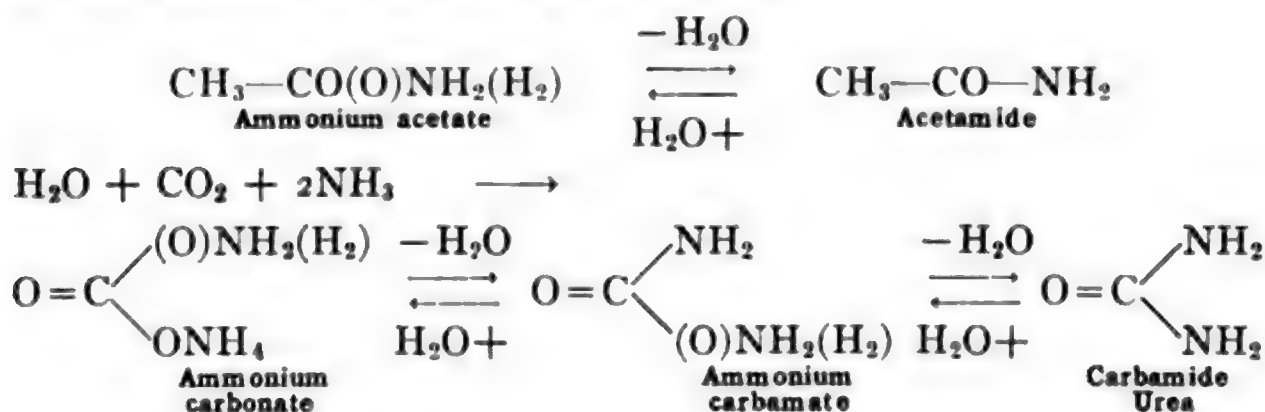


This reaction is similar to that which takes place when ammonia forms an addition product with aldehydes, e.g., ammonium acetaldehyde

(p. 116). **Ethyl carbamate** is formed by the action of ammonia upon ethyl chlor formate.



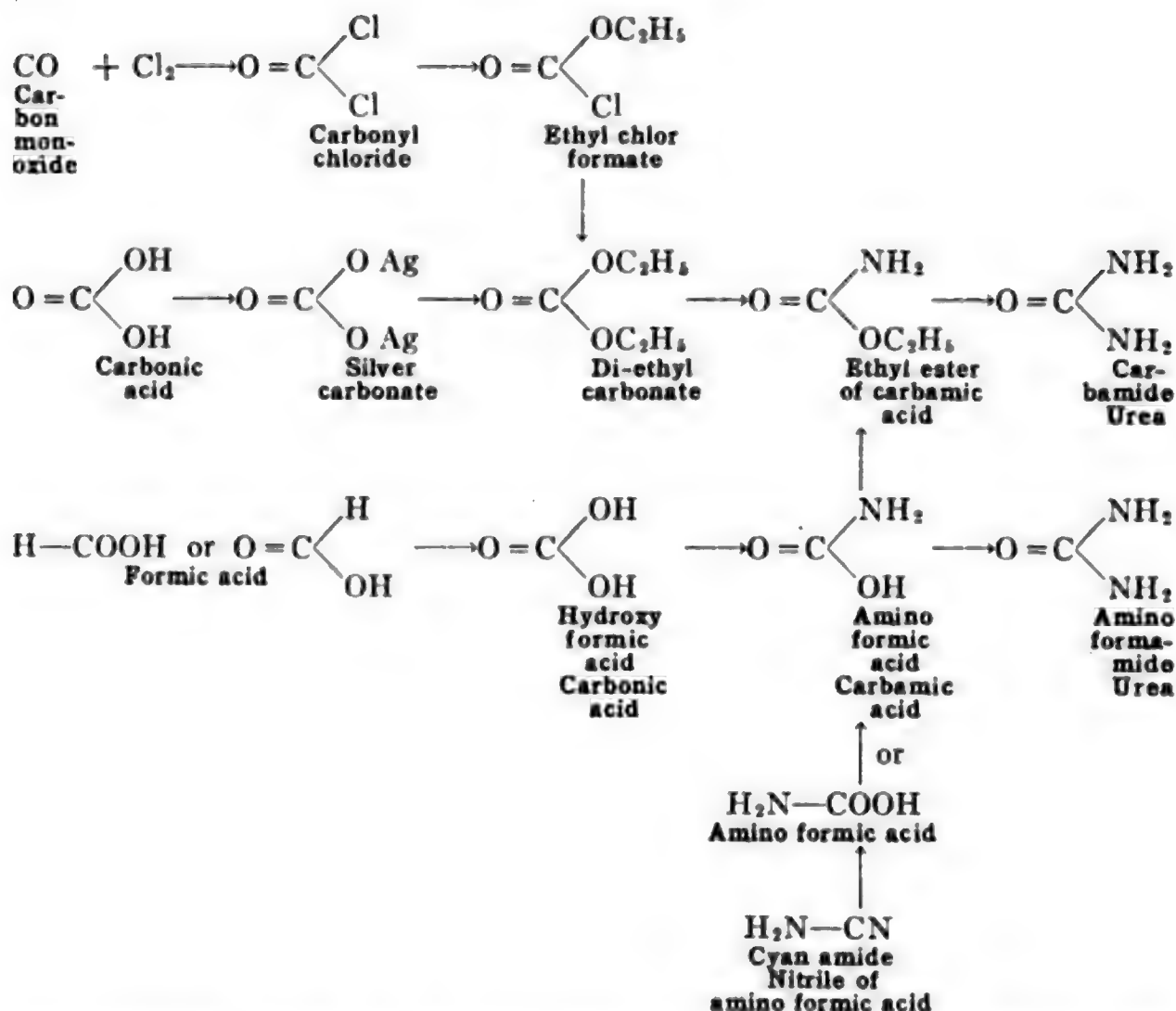
Urethane.—This ethyl ester of carbamic acid is known as **urethane**. Ammonium carbamate is the intermediate product in the relationship between ammonium carbonate and carbamide, analogous to that between ammonium acetate and acetamide.



As ammonium carbonate is formed by the action of ammonia and carbon dioxide this relationship agrees with the formation of ammonium carbamate just referred to.

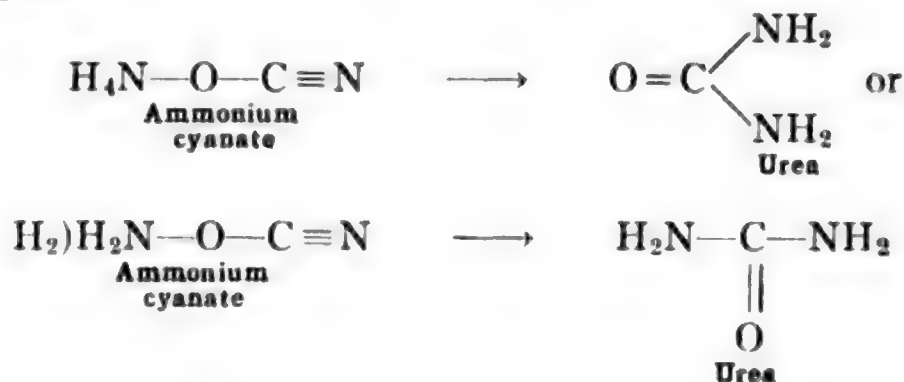
Biological Synthesis and Decomposition.—This relationship between urea and ammonium carbonate (ammonia and carbon dioxide) is of especial importance because it is concerned as a reversible reaction both in the synthesis of urea in the animal body and in the decomposition of urea in the soil. It is at least possible that the formation of urea in the animal body takes place, by the steps represented in the above relationship, from ammonia and carbon dioxide both of which are produced by the katabolic hydrolysis and oxidation of proteins. The reverse reaction, viz., the decomposition of urea into ammonia and carbon dioxide is taking place continually whenever urea in manure is being decomposed. In this way the greater part of the nitrogen of protein food is returned to the soil to be used as plant soil food.

If we consider together the facts which we have presented in regard to **urea** and **carbamic acid** we will realize that they are directly related to both **carbonic acid** and **formic acid**. The following schematic representation of these relationships will make this clear.

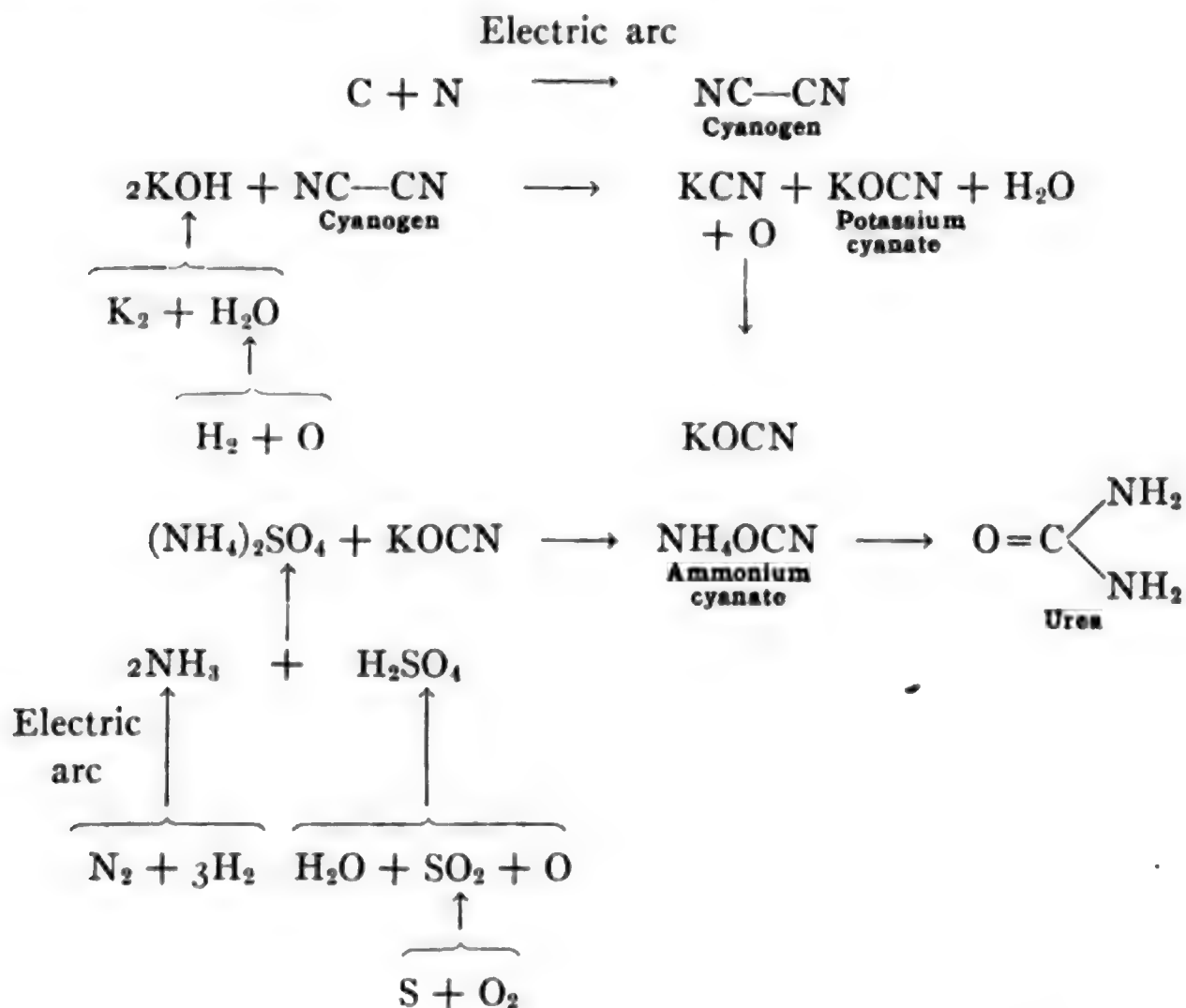


Thus **carbamic acid** may be considered either as **amino formic acid** or as the *mon-amide* of **carbonic acid**, *i.e.*, **carbamic acid**; and **urea** may similarly be considered as the *amide* of **amino formic acid** or as the *di-amide* of **carbonic acid**, *i.e.*, **carbamide**.

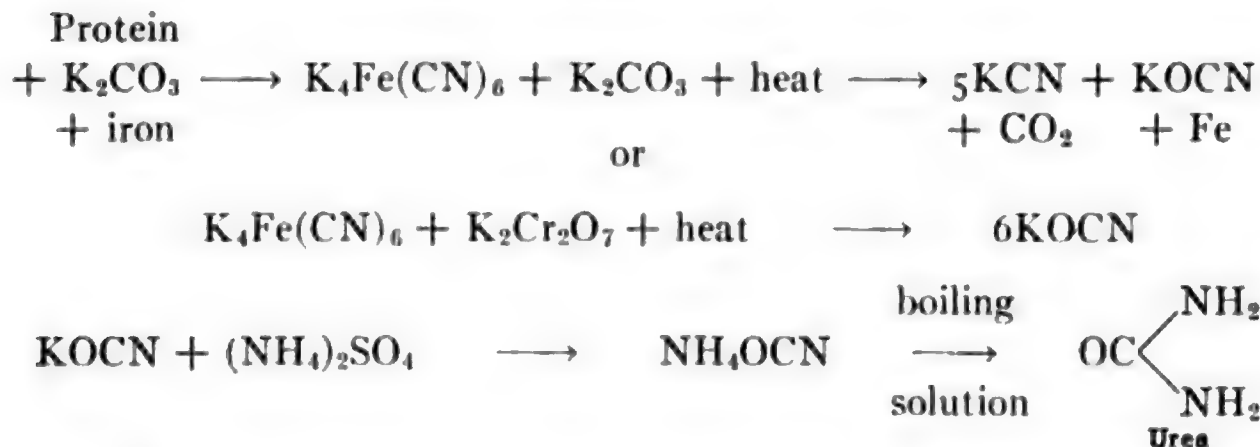
Wöhler's Synthesis.—From the preceding discussion of the constitution of urea and of ammonium cyanate (p. 418) we can express the transformation involved in **Wöhler's** synthesis of urea by the following rearrangement.



Recalling the methods of preparing hydrogen cyanide, we see how we may say, that, in **Wöhler's** synthesis, an animal substance was made from elemental constituents by laboratory methods.

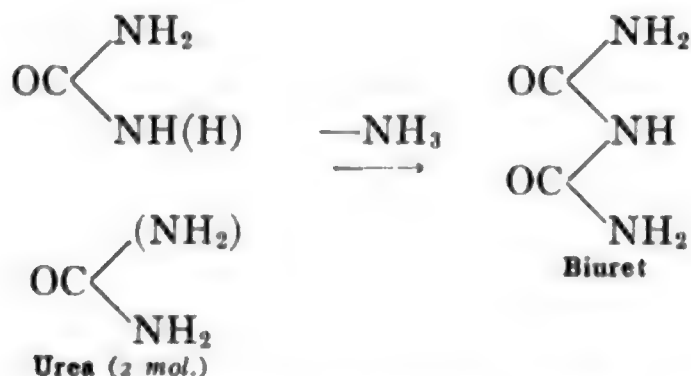


In the synthesis of urea from ammonium cyanate the cyanate may be used as such already prepared or it may be obtained from ferro-cyanides or cyanides by the transformations already given (p. 416).

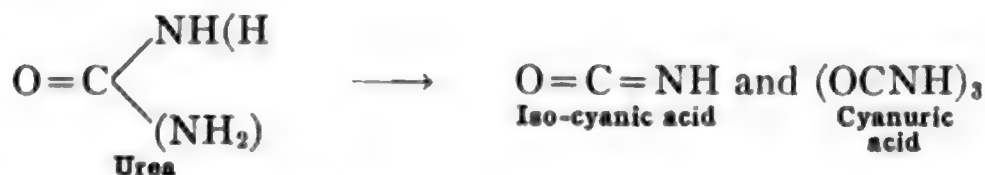


Occurrence and Properties.—Urea occurs as a normal constituent in animal urine to the amount of about 2 per cent in man. It was discovered in 1773. Its physiological significance will be considered later. It is also found in small amounts in the blood and lymph of animals. In the blood of sharks it is present in as large amounts as in human urine. Urea is a beautifully crystalline solid easily soluble in water and in alcohol. It melts at 132° – 133° and sublimes in a vacuum at 120° – 130° .

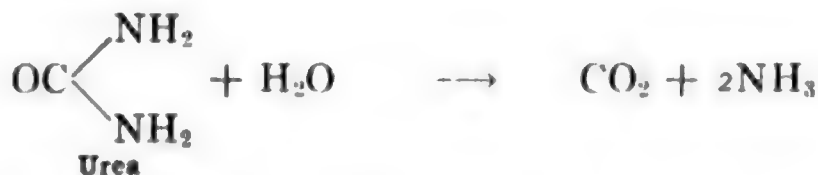
Biuret.—On further heating in the air it decomposes yielding carbon dioxide, ammonia, and an interesting body known as **biuret**. The last compound has the constitution shown by the following reaction. It is formed from urea by the loss of *one molecule of ammonia from two molecules of urea*. The significance of the name biuret is apparent from the reaction.



Also when urea loses *one molecule of ammonia from one molecule of urea* by the action of phosphorus pentoxide we obtain **cyanuric acid** and **iso-cyanic acid** (p. 418).



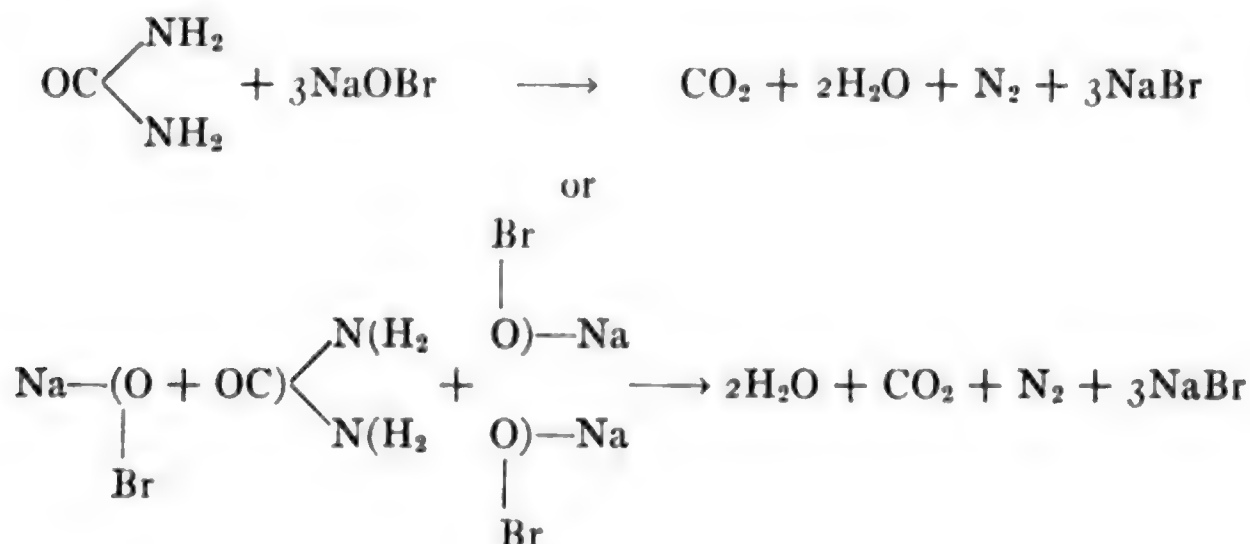
When boiled with acid or alkalies urea is decomposed into carbon dioxide and ammonia



Enzymatic Hydrolysis.—This is a simple hydrolytic reaction and is also brought about by enzymes and bacteria, so that when urine de-

composes by fermentation in piles of animal manure the urea yields carbon dioxide and ammonia which of course yield ammonium carbonate. The relation of urea to ammonium carbonate has been discussed (p. 431).

Hypobromite Reaction.—When treated with hypobromites or nitrous acid urea is oxidized and carbon dioxide water and **nitrogen** gas are obtained.



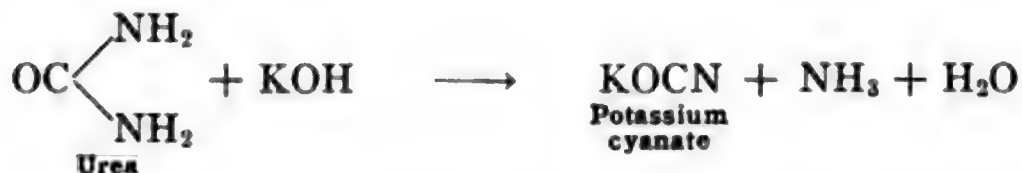
In this reaction *all of the nitrogen gas is set free, quantitatively, one molecule of nitrogen per one molecule of urea, (i.e.) 60 parts urea (mol. wt. urea = 60) yield 28 parts nitrogen (mol. wt. N. = 28).*

With nitrous acid twice the amount of nitrogen is obtained.



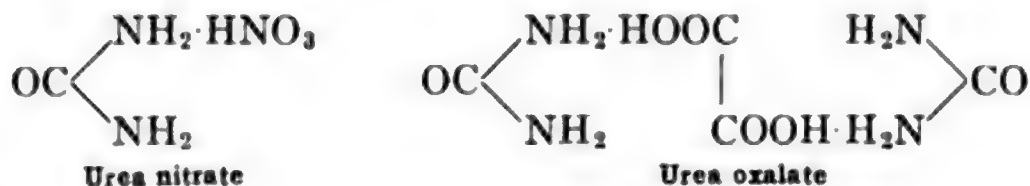
Clinical Test.—By these reactions, which are easily carried out by simply adding a sodium hypobromite solution to a solution of urea (urine), the per cent of urea in urine may be determined. The volume of the nitrogen gas evolved may be readily measured and from this the weight calculated. Apparatus made especially for this purpose, in which the volume of nitrogen gas evolved is read directly in per cent urea in the urine, are termed *ureometers* and give us simple clinical means of analyzing urine for urea. The sodium hypobromite solution is made up alkaline so that the carbon dioxide which is also evolved is absorbed, the nitrogen only remaining as a gas.

By heating with alcoholic potassium hydroxide urea yields potassium cyanate.

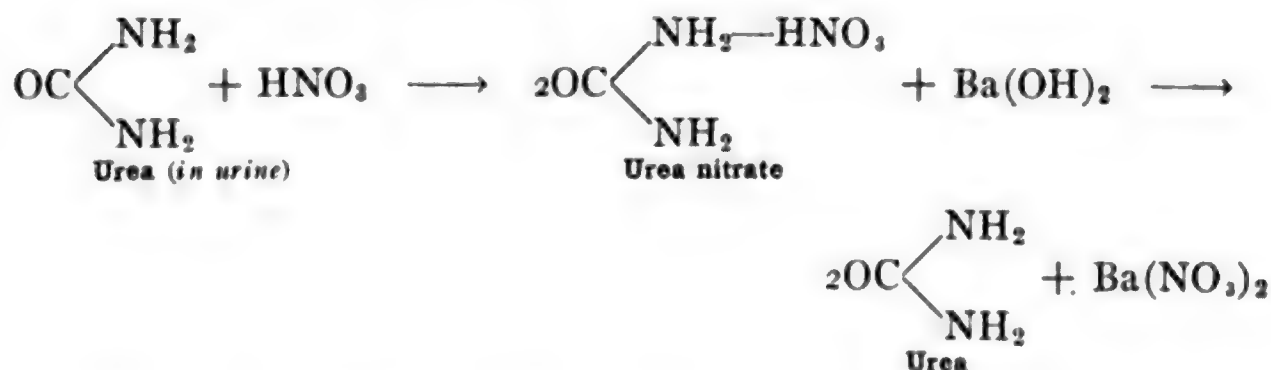


This is really the reverse of **Wöhler's** synthesis as ammonium cyanate may be considered as first formed.

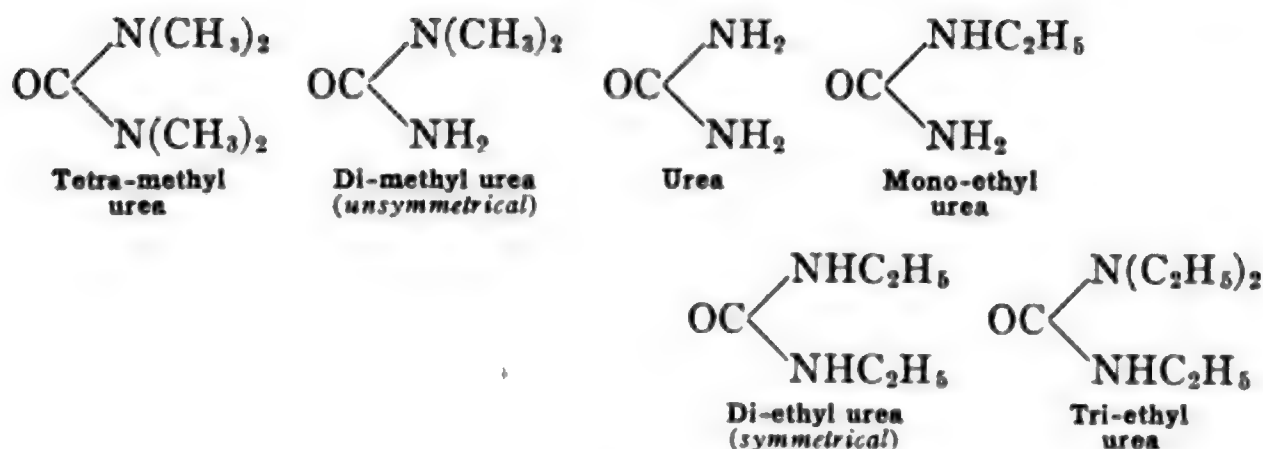
Salts.—Urea being a di-amide or an amino amide forms salts with acids, in which only *one* amino group is neutralized.



Isolation from Urine.—Urea may be easily isolated from urine by first converting it into the nitrate which is much less soluble and therefore crystallizes out. Urine is evaporated to a thin syrup and concentrated nitric acid added when urea nitrate separates in abundant crystals. These are purified by recrystallization and decolorization and then decomposed with barium hydroxide.



Alkyl Ureas.—By substituting alkyl amines for ammonia in the reaction for the synthesis of urea from carbonyl chloride, or by using alkyl derivatives of ammonium cyanate (cyanic acid salts of alkyl amines), in the **Wöhler** synthesis, **alkyl ureas** may be obtained. They are of different types as illustrated by the following formulas showing their relationship to urea.



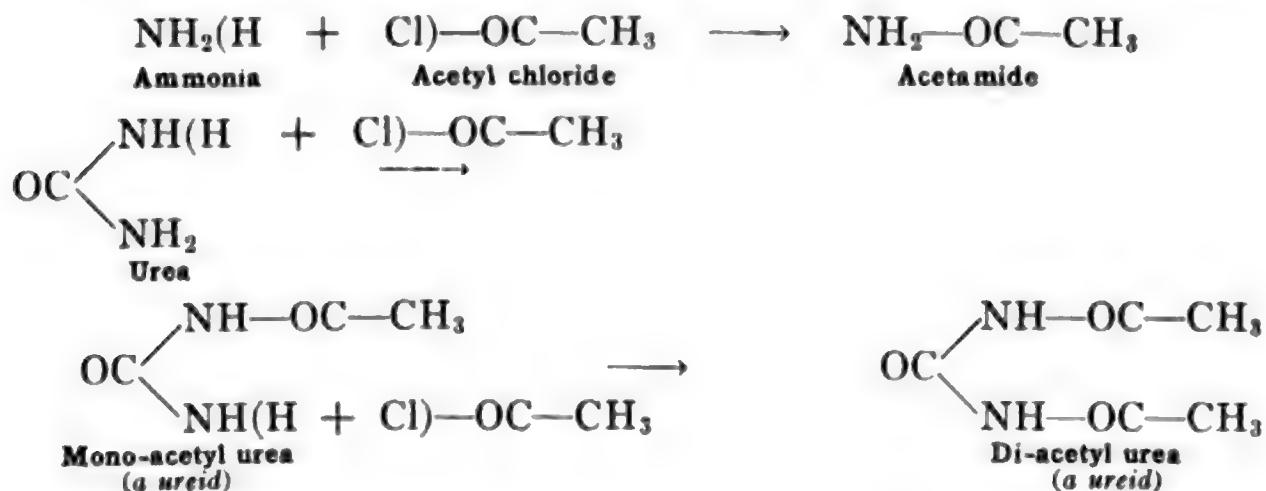
Thio-ureas

Thio-ureas.—As sulphur may replace oxygen in carbon dioxide, alcohol, carbonyl chloride and ammonium cyanate yielding corresponding *thio compounds*, so also there are sulphur analogues of urea known as **thio-ureas**. These need not be considered more than to give the oxygen and sulphur compounds in this relationship.

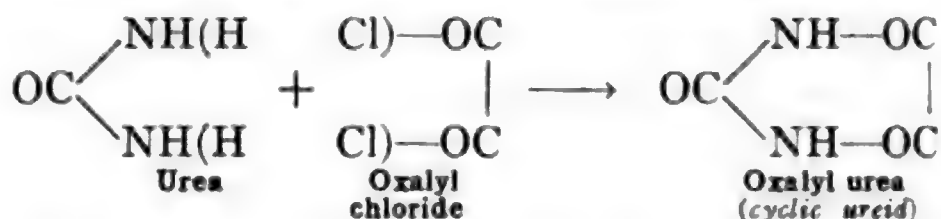
Ethyl alcohol	$\text{C}_2\text{H}_5\text{—OH}$	$\text{C}_2\text{H}_5\text{—SH}$	Thio-alcohol (<i>mercaptan</i>)
Carbon dioxide	CO_2	CS_2	Carbon di-sulphide
Carbonyl chloride	Cl—CO—Cl	Cl—CS—Cl	Thionyl chloride
Ammonium cyanate	$\text{NH}_4\text{—O—CN}$	$\text{NH}_4\text{—S—CN}$	Ammonium thio-cyanate
Urea	$\text{H}_2\text{N—CO—NH}_2$	$\text{H}_2\text{N—CS—NH}_2$	Thio-urea
Carbamic acid ester	$\text{H}_2\text{N—CO—OR}$	$\text{H}_2\text{N—CS—OR}$	Thio-carbamic acid ester
Alkyl urea	RHN—CO—NHR	RHN—CS—NHR	Alkyl thio-urea

Ureids

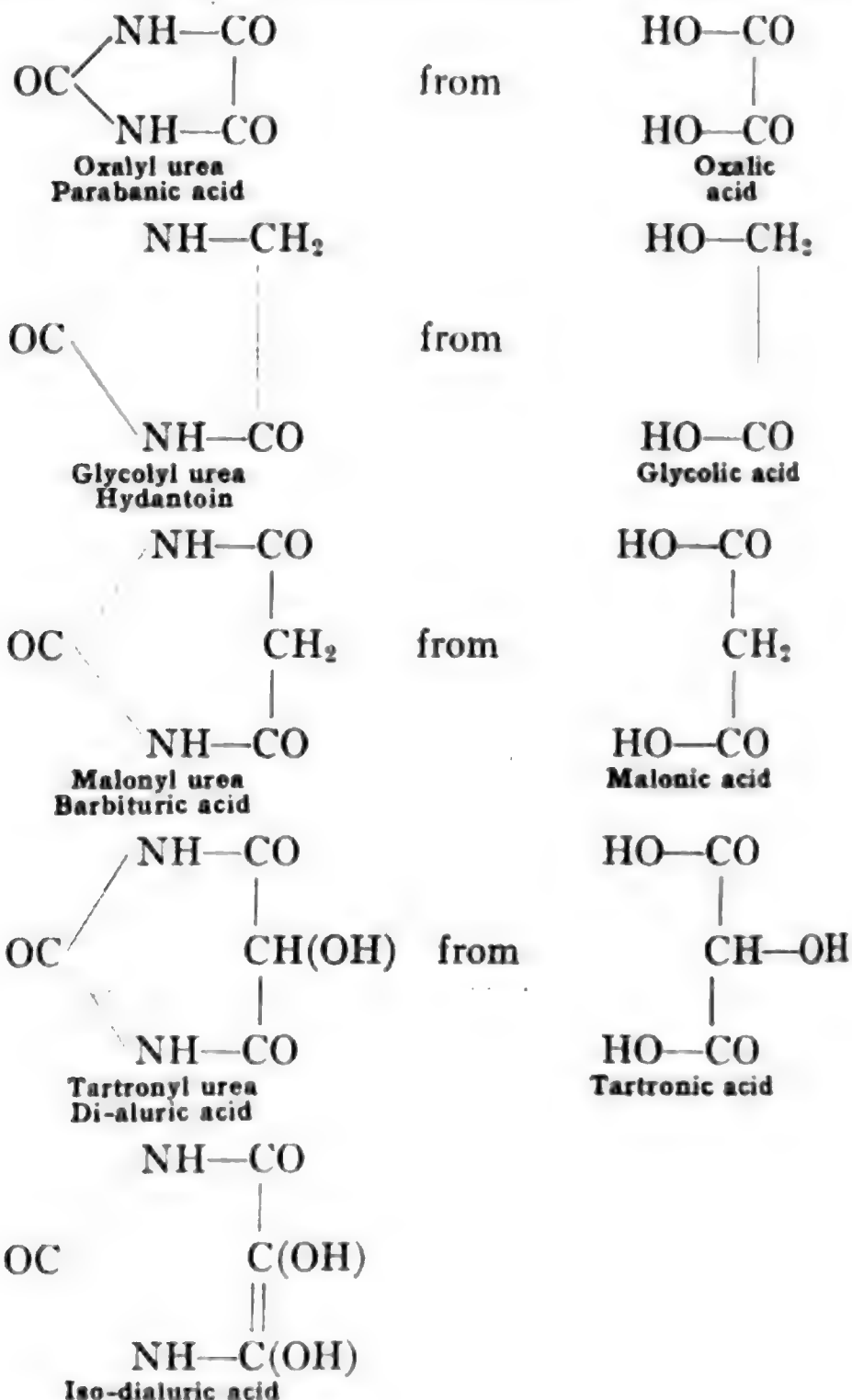
As an amino compound urea acts with acetyl chloride or acetic anhydride or other acyl-chlorides or anhydrides forming acyl derivatives analogous to acetamide. These compounds are termed **ureids**.

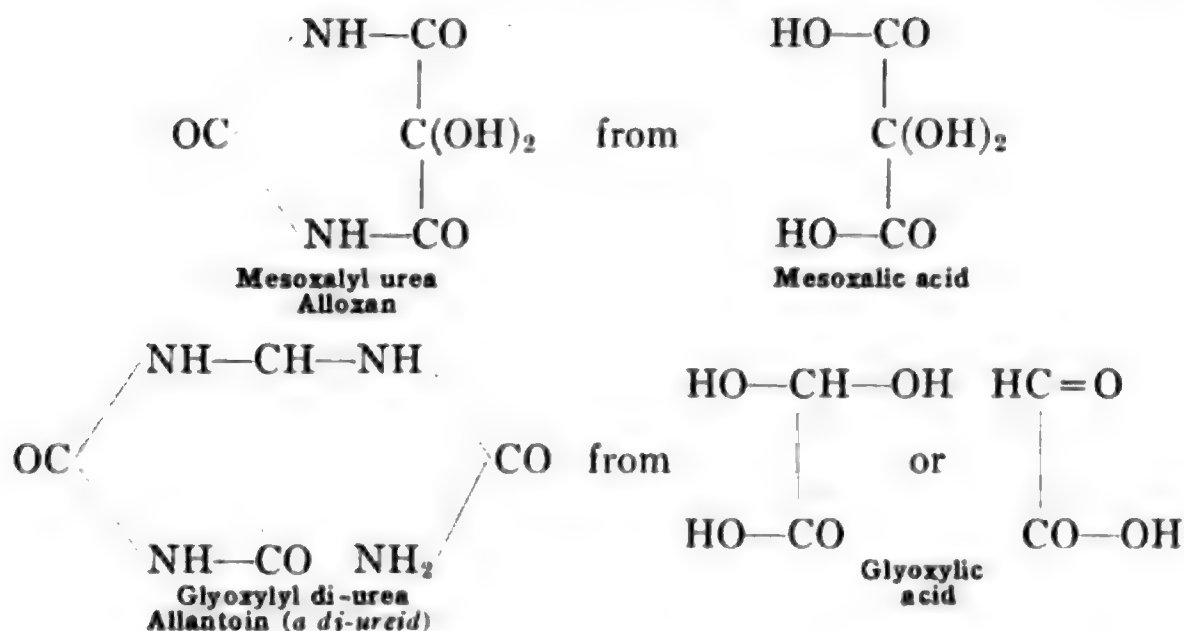


Cyclic Ureids.—With chlorides of di-basic acids, or of hydroxy mono-basic acids, the double acyl group unites with the two amino residues of urea forming a cyclic ureid as follows:



Several of these cyclic ureids are of especial importance in connection with uric acid which we shall presently discuss. These are as follows:

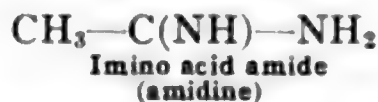
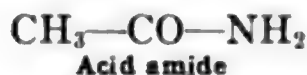
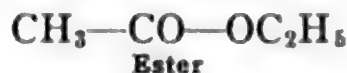




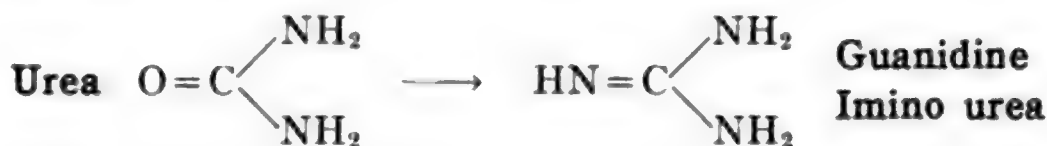
These compounds need not be discussed further than to show their relationships as above.

Imino Derivatives of Urea

The imino group ($=\text{NH}$), the bivalent ammonia radical, corresponds to bivalent oxygen and compounds result from the replacement of carbonyl oxygen with this *imino radical*. We have, for example, *imino esters* and *imino acid amides*.

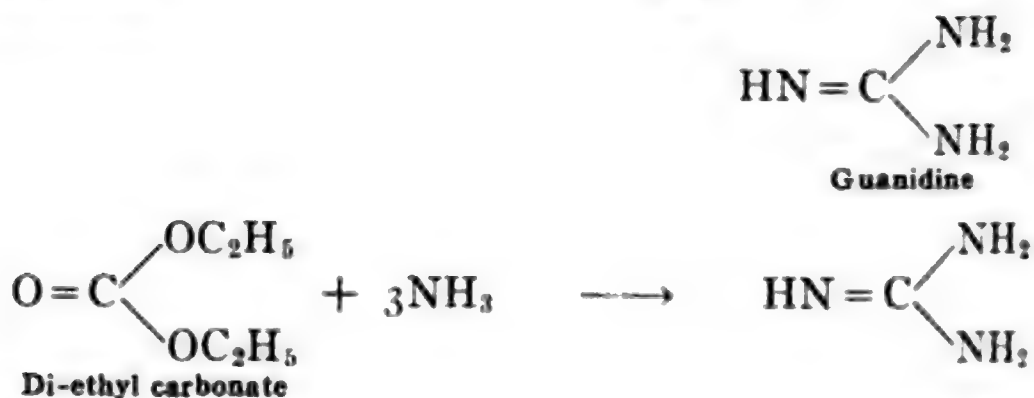
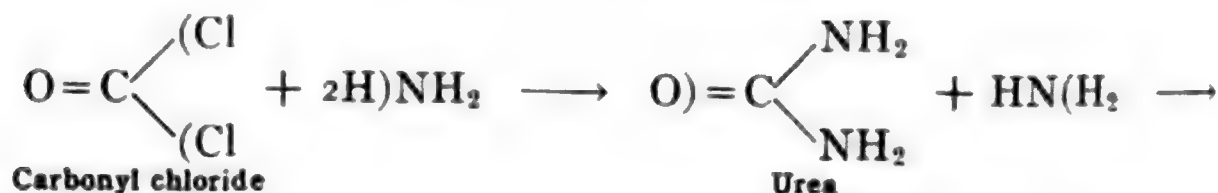


In urea the carbonyl oxygen is thus replaced by the imino group and an *imino urea* is obtained.

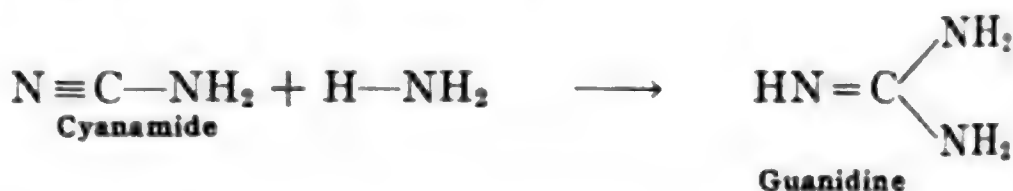


Guanidine, Guanine, Guano.—This compound is known as **guanidine**. It is obtained from a related compound known as **guanine** (p. 449), which is one of the nitrogenous compounds present in **guano**, a geological deposit of bird excrement and bird remains. Guano was at one time a valuable phosphate and nitrogen fertilizer. Guanidine has been prepared by analogous reactions to those used for the synthesis of urea, thus showing its relationship to urea, carbonic acid and

carbonyl chloride. It is formed by the more complete reaction of ammonia upon carbonyl chloride or upon carbonic acid esters.



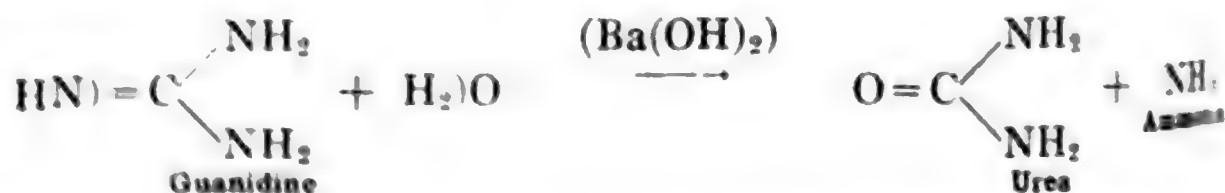
The most important synthesis of the compound is that from **cyanamide** by the direct addition of **ammonia**, when heated in alcoholic solution with ammonium chloride.



Similar to this last synthesis is that from **cyanogen iodide** and ammonia.

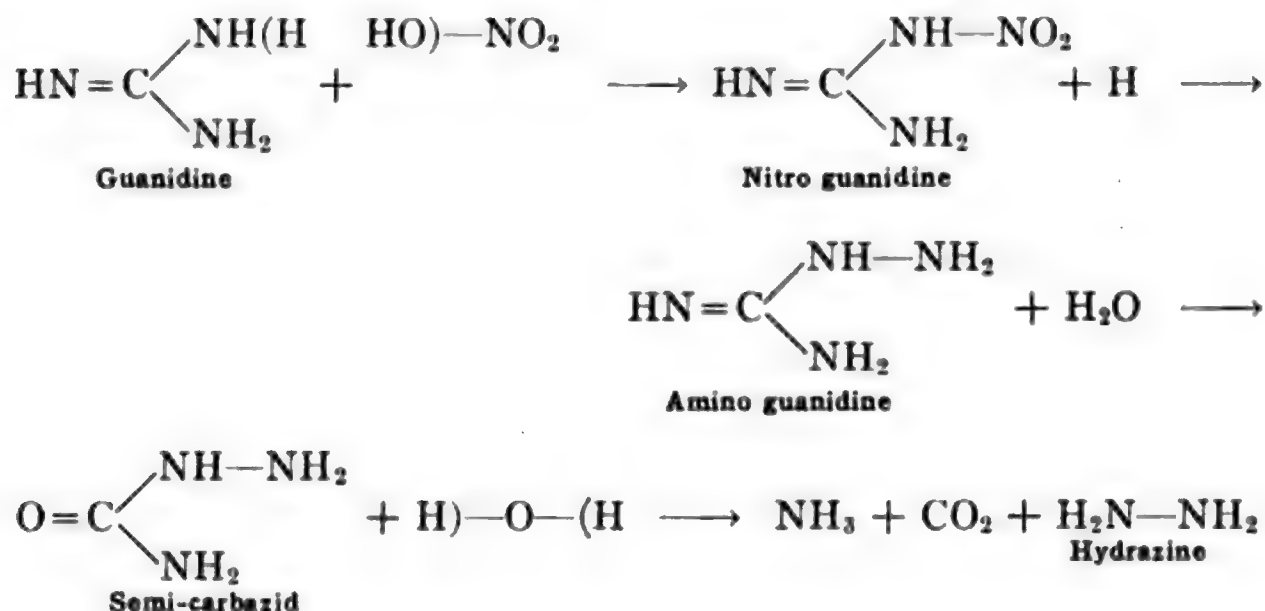


Guanidine is a soluble, crystalline compound and acts as a very strong base, as would be expected from the fact that it contains three ammonia residues, one of which, as an imino group, is in place of a carbonyl oxygen in urea or in carbonic acid. It readily absorbs carbon dioxide from the air. It is decomposed by barium hydroxide into urea and ammonia.

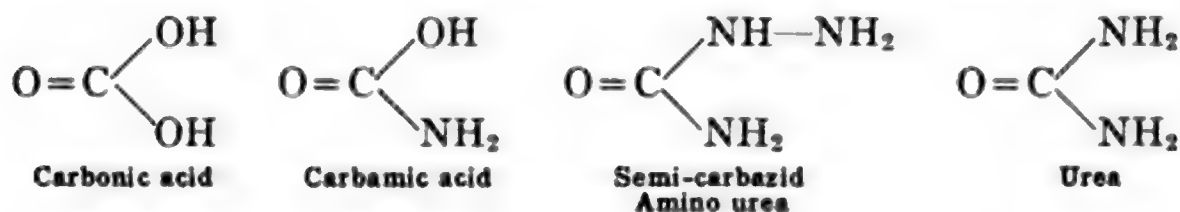


Being basic it forms salts with acids analogous to the urea salts.

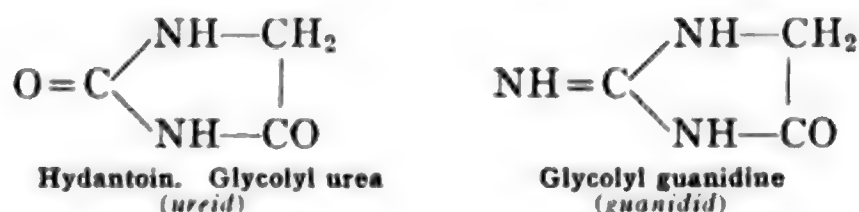
Semi-carbazid.—When guanidine is nitrated, by means of a mixture of nitric and sulphuric acids, a **nitro guanidine** is obtained, which, on reduction, yields **amino guanidine**, and this, on boiling with dilute acids or alkalis, yields a compound known as **semi-carbazid**. This in turn breaks down into **ammonia**, **hydrazine** (di-amine) and **water**.



Semi-carbazid is an important reagent forming derivatives with aldehydes and ketones. Its name indicates that it is a hydrazine derivative of carbonic acid or of carbamic acid. It is also **amino urea**.

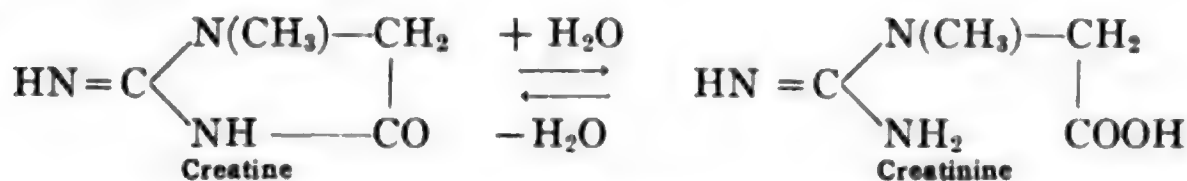


Corresponding to the ureids derived from urea by the action of acid chlorides, we have **guanidids** derived from **guanidine** by the same action.



Creatine and Creatinine.—This particular guanidid is important because the methyl derivative of it is a substance found in urine and

known as **creatine**. The non-cyclic guanidid corresponding to this is known as **creatinine**.



Plainly creatinine is the hydrate of creatine or, vice versa, creatine is the anhydride of creatinine. Both of these compounds are found in urine associated with urea as metabolic products of proteins.

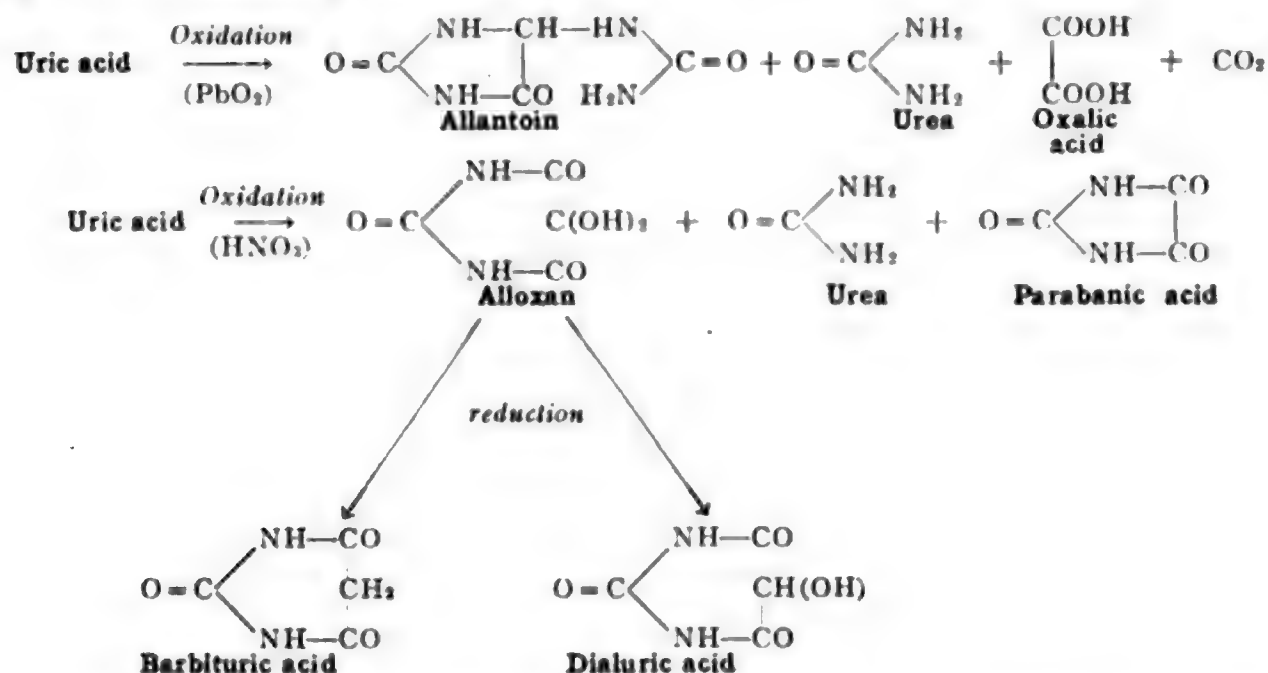
C. URIC ACID

Uric acid is associated with urea, creatine and creatinine in urine. In the urine of mammals it occurs in small amounts, the chief nitrogen compound being urea. In birds and reptiles, however, uric acid predominates and is the precursor of the related guanine in guano.

Constitution.—The constitution of uric acid has been established by a remarkable set of syntheses based upon a study of the products of decomposition. In this work several men played an important part. The most comprehensive work which cleared up the question of the constitution not only of uric acid but of several related compounds, which we shall presently consider, was by **Emil Fischer**, whom we have already mentioned in connection with two other groups of compounds intimately connected with plants and animals, viz., the **carbohydrates** and the **proteins** (p. 393). Earlier important work was done by **Liebig** and **Wöhler**, and the relationship of the decomposition products was mainly due to the work of **Baeyer**. The accepted formula was first suggested by **Medicus**, and the syntheses supporting it were worked out by **Horbaczewski**, and by **Behrend** and **Roosen**.

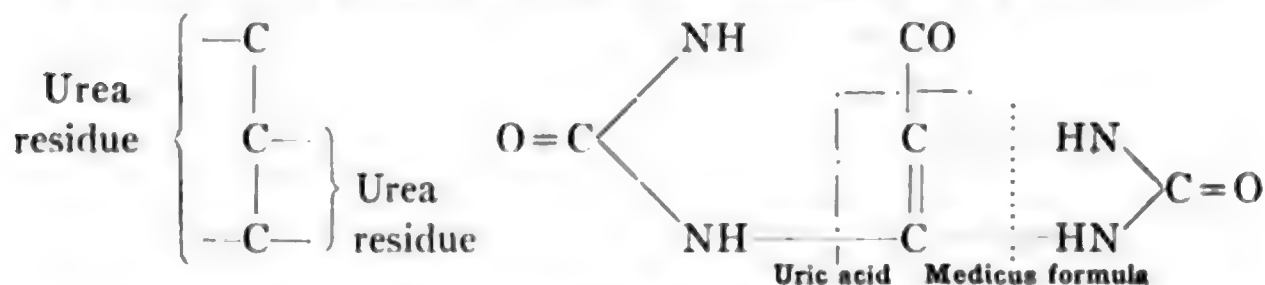
One of the first facts observed in regard to uric acid was that on heating it yielded **cyanuric acid**, $(\text{OCNH})_3$, and **ammonia**, NH_3 . As these same products had been obtained by heating **urea**, $\text{OC}(\text{NH}_2)_2$, it was considered probable that a *urea residue* was present in uric acid. It was then shown that on oxidation with lead dioxide, one of the ureids, the *di-ureid* known as **allantoin** was obtained, together with **urea**, **oxalic acid** and **carbon dioxide**. With other oxidizing agents, such as nitric acid, the products were equal molecules of **urea** and the two ureids **alloxan** and **parabanic acid**. From alloxan there may be obtained, by reduction, two other ureids, viz., **barbituric acid** and

dialuric acid. The established constitution of these ureids (p. 438) gives the following relationship.



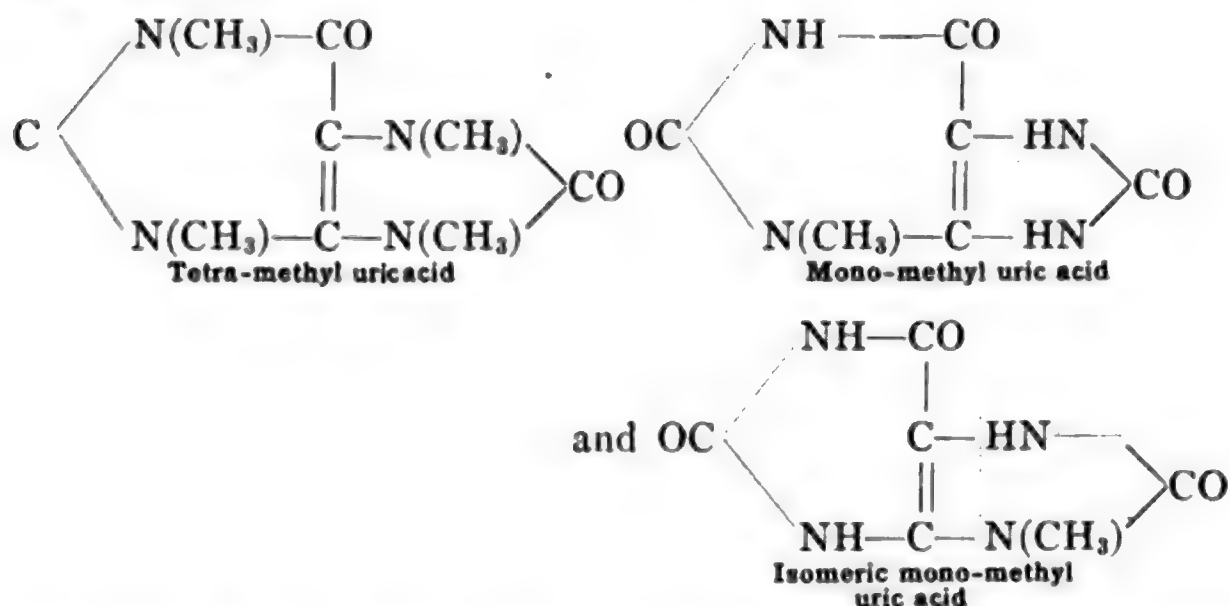
From the facts that uric acid yields the *di-ureid* allantoin and also equal molecules of alloxan, a *mono-ureid*, and **urea** it was concluded that uric acid must contain *two urea residues*. From the constitution of alloxan and its reduction products, barbituric and dialuric acids, uric acid must likewise contain a *three carbon chain linked to a urea residue by the end carbon atoms*. Also, as it yields parabanic acid or oxalyl urea, *one of the urea residues must be linked to two adjacent carbon atoms in this chain*.

Medicus' Formula.—The following grouping is thus indicated and will be seen to be present in the formula as suggested by **Medicus**.

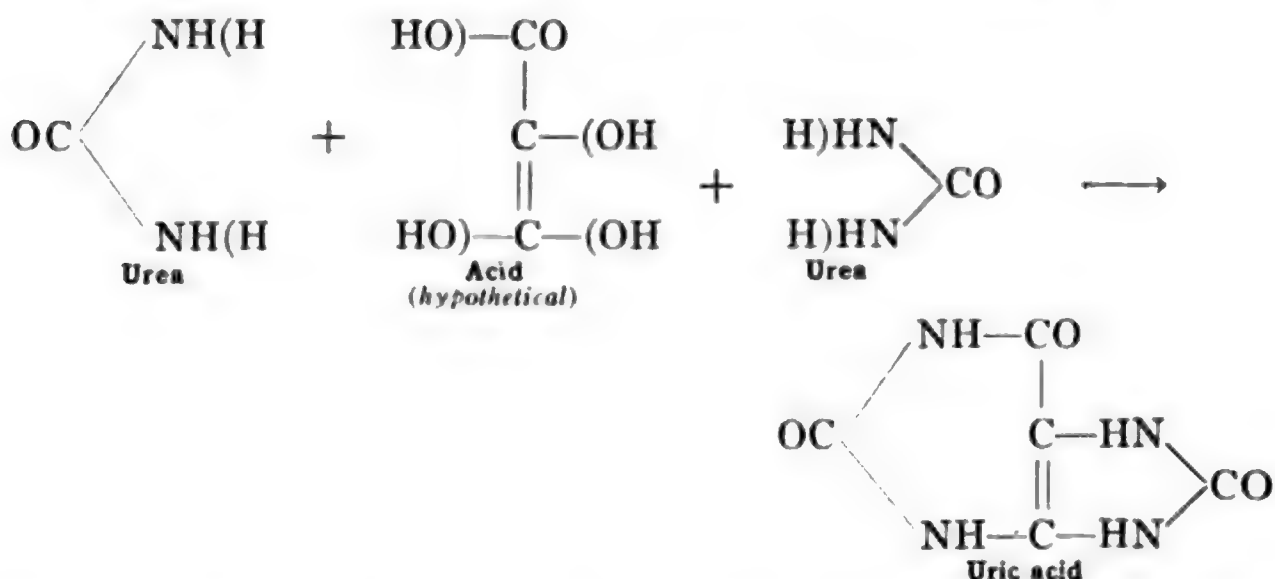


The splitting of the compound at the *dotted line* would yield **alloxan** and **urea** while splitting at the *broken line* would yield **parabanic acid** and **urea**. Confirmation of this constitution has been furnished in two ways: (1) by **Fischer's** study of the methyl substitution products of uric acid and (2) by the syntheses of **Horbaczewski** and of **Behrend** and **Roosen**.

Methyl Uric Acids, Fischer.—Fischer found two important facts in regard to the methyl uric acids. (a) There is a **tetra-methyl uric acid** in which *each methyl group is linked to a nitrogen atom* so that there must be *four imino hydrogen atoms in uric acid*. (b) There are two isomeric **mono-methyl uric acids**, therefore, *two of the imino groups must be unlike, i.e. the compound must be unsymmetrical*. These compounds are:



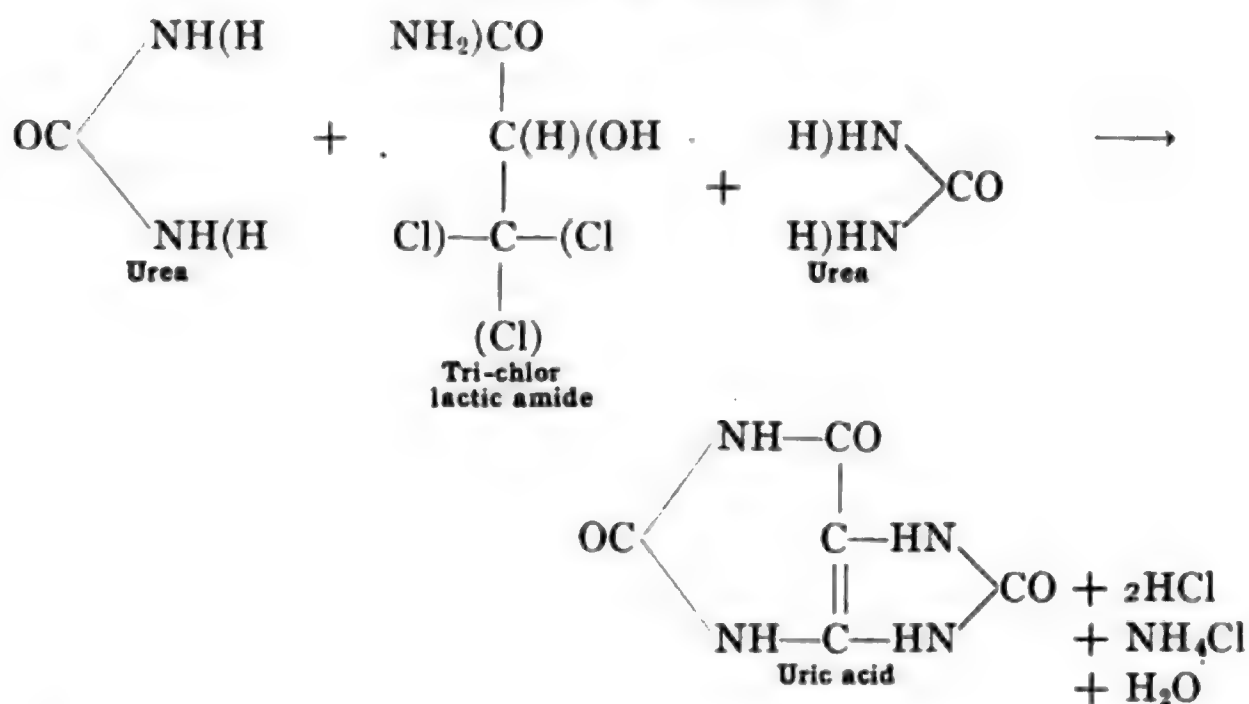
He found that one of these mono-methyl uric acids yielded **methyl alloxan** and **urea**, whereas the other yielded **methyl urea** and **alloxan**; as indicated by the *dotted lines*. Therefore uric acid is a *di-ureid* of an acid as represented below, the ureid being formed as follows:



Such an acid is not known, but it would be **tri-hydroxy acrylic acid**, $\text{C(OH)}_2=\text{C(OH)}-\text{COOH}$, from $\text{CH}_2=\text{CH}-\text{COOH}$, **acrylic acid**.

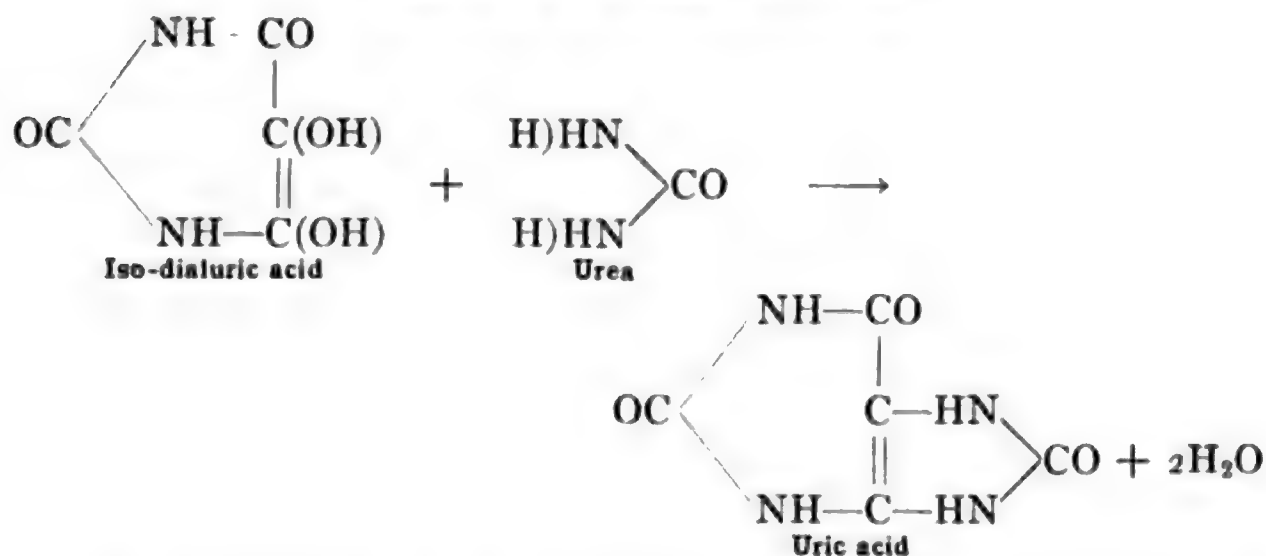
Horbaczewski's Synthesis.—The syntheses which establish the above formula are several. The two best are those before mentioned, of **Horbaczewski** and of **Behrend** and **Roosen**. The former heated together **tri-chlor lactic amide** and **urea** and obtained **uric acid**.

Horbaczewski's Synthesis



Behrend and Roosen's Synthesis.—The latter prepared uric acid by heating **iso-dialuric acid** and **urea** with sulphuric acid.

Behrend and Roosen's Synthesis



The constitution of the **iso-dialuric acid** was established by its synthesis from **aceto-acetic ester** and **urea**.

Properties.—Uric acid forms colorless crystals which are only slightly soluble in water. One part requires 1900 parts boiling water and 10,000 parts at 18.5°. Therefore in urine it can not be present as free uric acid above 0.01 per cent, while as a fact it is present to about five times that amount, viz., 0.05 per cent. It is probable that it is present in urine not as free acid but as salts of sodium or potassium. These salts of uric acid are soluble. When acid fermentation of urine occurs the uric acid crystallizes out as a characteristic sediment. It is obtained from urine by acidifying when on standing the uric acid separates in more or less colored crystalline masses. It is readily soluble in lithium carbonate and this compound is used medicinally for dissolving uric acid in the form of urinary calculi which consist sometimes largely of uric acid and insoluble urates. Uric acid reduces Fehling's solution slightly.

PHYSIOLOGICAL RELATIONS OF UREA, URIC ACID, ETC.

Urine Nitrogen.—The nitrogen compounds which we have been discussing, viz., **urea**, **uric acid**, **creatine** and **creatinine** are all present in animal urine. The nitrogen present in all of these substances comes from **protein** material. They are the waste or excretion products of body and food protein. When the protein of the animal cells is oxidized by means of the oxygen in the blood, whereby energy is produced, the **nitrogen** of the protein thus oxidized is converted ultimately into one of the compounds named. As these compounds are themselves oxidizable, not all of the energy of the protein substance is liberated by the oxidation in the cell. These urea compounds are not, however, further oxidized in the body but are conveyed by the blood to the kidneys from which they are eliminated in the urine as excretion products. These are not the only nitrogenous constituents of urine but they constitute by far the larger proportion of the *total nitrogen compounds present*. In mammalian animals urea is the predominating nitrogenous substance and it is present sometimes in an amount equal to over 90 per cent of the total metabolized protein nitrogen. This proportion varies with the total metabolized protein nitrogen excreted, for when the total nitrogen is reduced the proportion of that nitrogen eliminated as urea is decreased to 60 *per cent* and in pathological cases has fallen as low as 14 *per cent*. The amount of urine excreted

per day by the average man (American) is 1000–1200 cc. In this urine about 16 *grams of metabolized nitrogen* are present and of this 16 grams, 14 grams are present as urea, and 0.6 gram as uric acid, 1.0 gram as creatinine and creatine, 0.7 gram as ammonia and 0.004 gram as other organic nitrogen compounds known as **purine bases** which we shall next consider.

Urine nitrogen	Urea	14.0 g.
per day = about 16 g.	Uric acid	0.6
in 1000–1200 cc.	Creatinine	1.0
urine	Creatine	
	Ammonia	0.7
	Purine bases	0.004
		<hr/>
		16.304

This amount of nitrogen represents approximately 100 *grams of protein* which is the average amount of protein food metabolized per day.

Urine Analysis.—The determination of the amounts of these nitrogenous compounds in urine, especially of urea and uric acid, is important in physiological investigations. The quantitative determination of urea is accomplished by some form of sodium hypobromite decomposition, as already discussed (p. 435). The uric acid is best determined by converting it into the insoluble ammonium urate, separating it as such, converting the ammonium urate into uric acid by means of sulphuric acid and titrating the uric acid with potassium permanganate.

In urine two other substances which do not contain nitrogen are of especial importance as pathological constituents.

Sugar and Albumin in Urine.—**Sugar (glucose)** occurs in urine in the case of the disease known as *diabetes mellitus*. The qualitative test and quantitative determination of glucose by means of *Fehling's solution* (p. 332) are the methods usually employed. Normal urine gives no glucose test with Fehling's solution. Uric acid interferes slightly with this test as it does reduce Fehling's solution to some extent.

Albumin.—The presence of albumin (protein) in urine is also pathologic. It is tested for most easily by what is known as *Heller's ring test*. About 2–5 cc. urine are introduced into a narrow or conical test glass. An equal volume of concentrated nitric acid is then carefully

introduced beneath the urine by means of a pipette. On standing a cloudy ring appears at the zone between the two liquids in case albumin is present.

D. PURINE BASES

A group of very interesting naturally occurring compounds are known which are nitrogenous basic substances and which are related to uric acid. They are:

Caffein

or

from coffee or tea

Theine

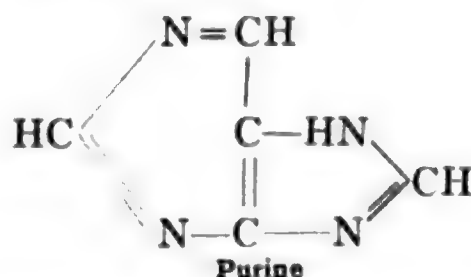
Theobromine from cacao

Xanthine from urine

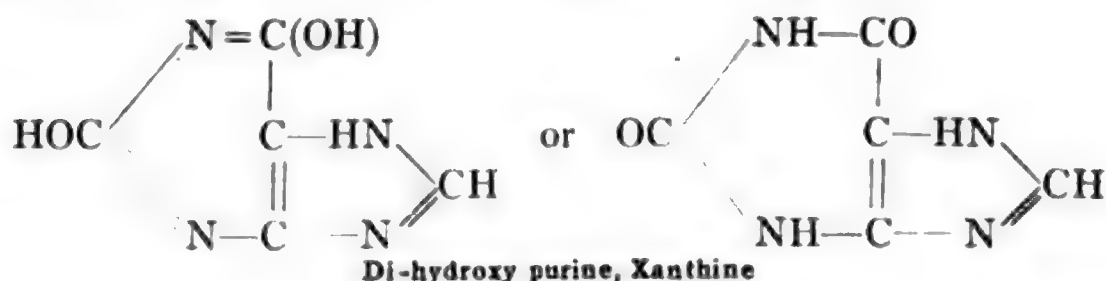
Guanine from guano

From his work on uric acid **Fischer** was led to study these bases. He showed that they are directly related to uric acid and the proof of their constitution cleared up the whole question in regard to uric acid. It will be unnecessary here to go into detail in regard to the various syntheses and reactions by which this relationship was established. Suffice it to give the conclusions.

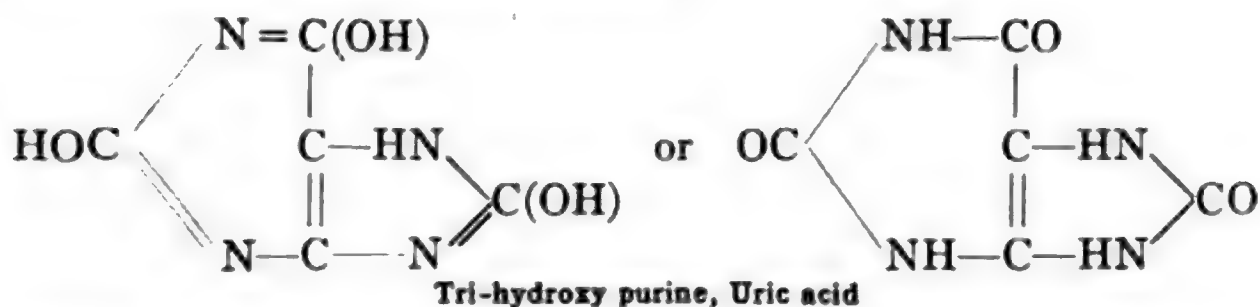
Purine.—**Fischer** found that all five compounds were related to a carbon, hydrogen, nitrogen substance which he prepared and called **purine**. It was shown to be



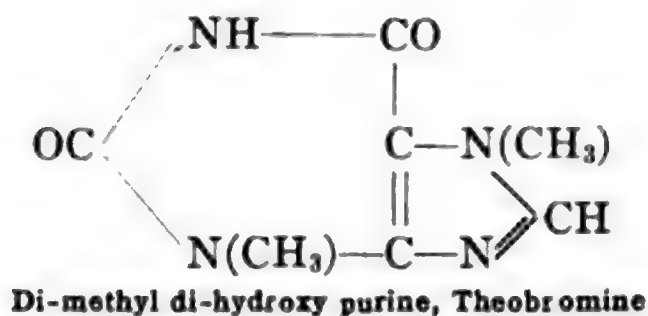
Xanthine was shown to be a di-hydroxy purine.



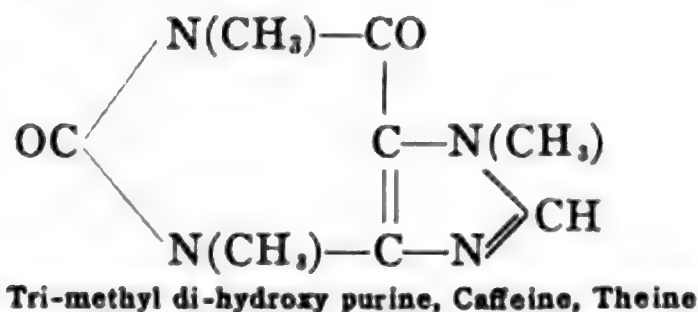
Uric acid is tri-hydroxy purine.



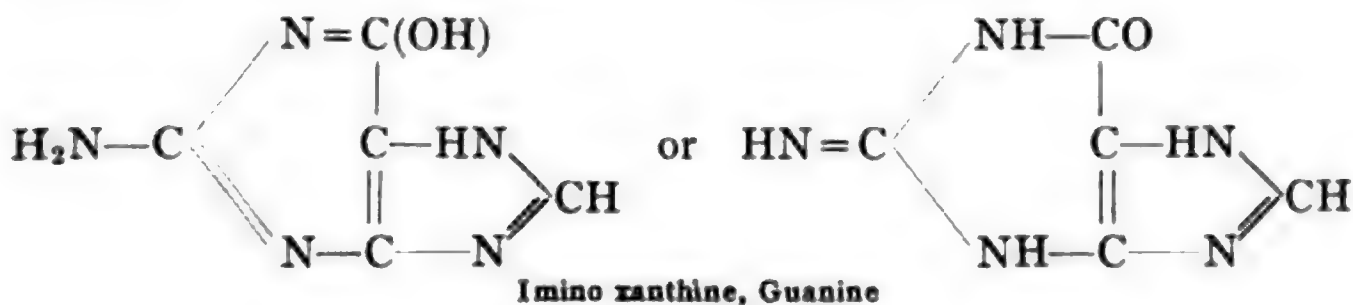
Theobromine was shown to be di-methyl xanthine or di-methyl di-hydroxy purine.



Caffeine and theine were shown to be tri-methyl xanthine or tri-methyl di-hydroxy purine.



Guanine is the *mono-amino* or *mono-imino* compound corresponding to xanthine, *i.e.*, imino xanthine or mono-amino mono-hydroxy purine.



Guanine, therefore, would yield guanidine as well as urea (p. 439).

The assigning of the two types of formulas in some cases, *i.e.*, the hydroxyl or *alcohol formula* (*enol formula*) and the ketone or *carbonyl formula* (*ketone formula*), is due to the fact, not mentioned in the case of uric acid, that it is probably a *tautomeric* compound

existing sometimes in one form and sometimes in the other. The hydroxyl formula for xanthine seems to be excluded by the fact that in it only *one imino hydrogen* remains, whereas three methyl groups may be introduced in forming caffeine, the tri-methyl xanthine. In the ketone or carbonyl formula three such imino hydrogens remain.

Other nitrogen bases, also shown to be purine derivatives, have been discovered, *e.g.*, **hypoxanthine**, **adenine**, **theophylline**. All of these purine compounds will be referred to again under **alkaloids** (Pt. II), for they really belong in that group. Their relation to urea, however, has made it desirable to discuss them at this time.

PART II
CYCLIC SERIES

PART II

CYCLIC SERIES

INTRODUCTION

RESUMÉ OF ALIPHATIC SERIES

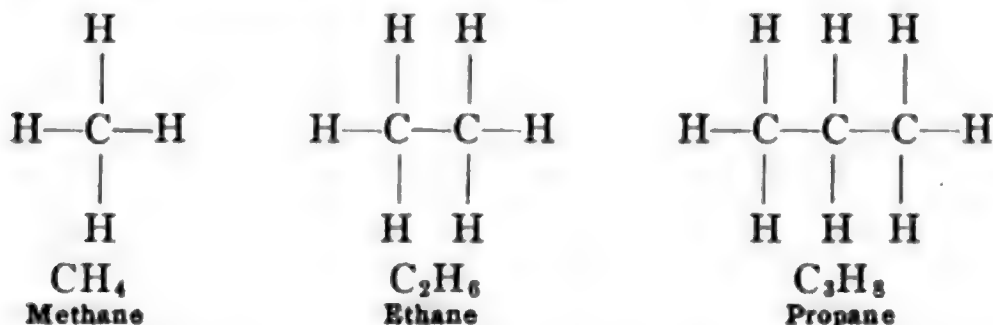
We come now in our study to a very distinct and very remarkable division. All of the compounds which we have thus far considered belong to what we have termed the **aliphatic series** and are genetically related to **methane**, the simplest representative. They possess certain similar properties and are represented by constitutional formulas which are characteristic of the entire series. The compounds which we are now to study, and which are related to a hydrocarbon known as **benzene**, exhibit certain fundamental properties which are distinctly different from those characterizing the members of the aliphatic series, and they are represented by constitutional formulas of a distinctly different character. It is customary, therefore, to classify organic compounds into two large divisions, making the separation at this point.

It must not be inferred, however, that we shall find nothing in common in the compounds of the two divisions. Just as there is no sharp line of separation between the two classes of compounds, *inorganic* and *organic*, so, we shall find, there is no hard and fast line separating the divisions we are now making. Certain transition compounds serve as a link between the two, and the compounds of this new group may also be truly considered as genetically derived from **methane**. Also, we shall find among these new compounds representatives of such groups as **alcohols**, **aldehydes**, **acids**, etc., and as such they possess the properties characteristic of these groups. It may thus be considered as a question whether the similarities between the two sets of compounds are not of more fundamental importance than the distinctive differences and whether it is not more desirable to consider them all together than to make the usual division. However, for the purpose of teaching it seems far better to adhere to the classification commonly adopted.

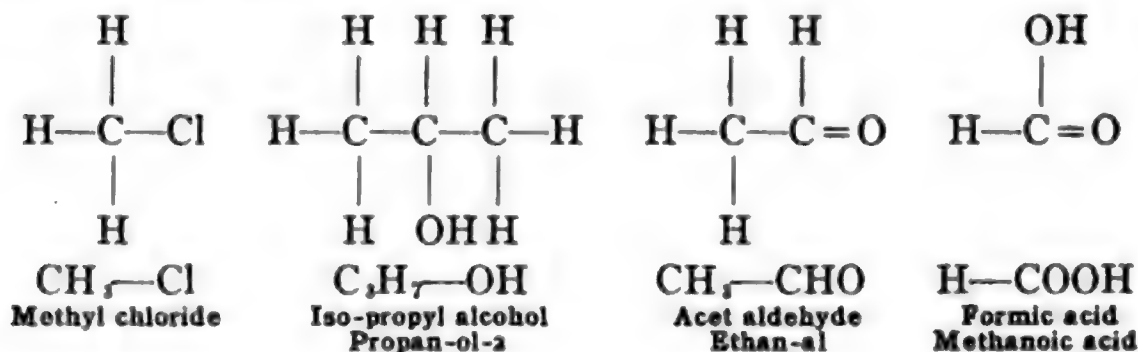
It will be well before taking up this new series of compounds to

glance briefly at certain prominent characteristics of the aliphatic series in order to emphasize those points which are distinctive, especially such as have to do with our ideas of constitution.

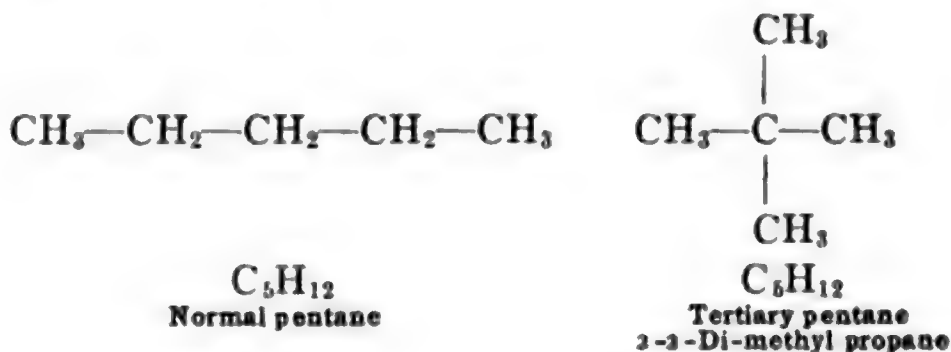
The *paraffin* or aliphatic series of hydrocarbons and their derivatives possess constitutions represented by structural formulas in which the carbon atoms are linked together in an *open chain* formation. For the hydrocarbons themselves such structural formulas, written on a plane surface, may be illustrated as follows:



The derivatives of these hydrocarbons result from the substitution of some monovalent or polyvalent element or group of elements in place of one or more hydrogen atoms. Such compounds may be illustrated by the following:



While the chain of carbon atoms may become more or less branched it always remains an *open* chain. Examples of straight and branched chains may be given by two of the isomeric pentanes.



All of these examples are compounds which belong to what are termed the *saturated* series. In the *unsaturated* series the compounds also have a constitution represented by formulas of this same open chain character; but, in them, one or more pairs of carbon atoms are doubly or triply linked, as follows:

$\text{CH}_2 = \text{CH}_2$,	Ethylene or Ethene ,	C_2H_4
$\text{CH}_3 - \text{CH} = \text{CH}_2$,	Propylene or Propene ,	C_3H_6
$\text{CH} \equiv \text{CH}$,	Acetylene or Ethine ,	C_2H_2
$\text{CH}_3 - \text{C} \equiv \text{CH}$,	Allylene or Propine ,	C_3H_4
$\text{HC} \equiv \text{C} - \text{CH}_2 - \text{CH}_2 - \text{C} \equiv \text{CH}$, Di-propargyl , 1-5-hexa di-ine , C_6H_6		

The derivatives of these unsaturated hydrocarbons are wholly analogous to those of the saturated series, and differ from them, in structure, only as the hydrocarbons themselves differ, viz., in the double or triple linkage of some of the carbon atoms. In each group of similar hydrocarbons, and also in the derivatives of each group, we have a more or less numerous series of compounds each member of which differs from its predecessor in the series by a certain constant increase in the number of carbon and hydrogen atoms, viz., by CH_2 . Such series are known as *homologous series* and may be represented by general formulas, illustrated in the case of hydrocarbons themselves, as follows:

Saturated Hydrocarbons,	$\text{C}_n\text{H}_{2n+2}$
Ethylene Unsaturated Hydrocarbons,	C_nH_{2n}
Acetylene Unsaturated Hydrocarbons,	$\text{C}_n\text{H}_{2n-2}$
Dipropargyl	$\text{C}_n\text{H}_{2n-6}$

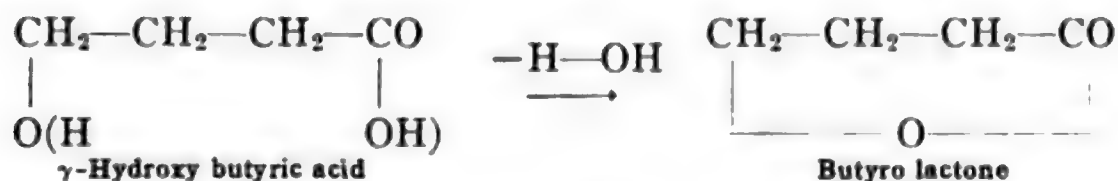
The relationships between these different series have been definitely established by means of reactions which enable us to pass from one series to another. Such reactions bring out a very important fact: that the hydrocarbons of the unsaturated series differ from those of the *saturated* series in a very definite way, viz., in the *formation of addition products*. These addition products, most readily formed with the halogens or halogen-hydro acids, are always the result of the addition of *two, four, or six* monovalent atoms to each unsaturated molecule, with the *conversion of the unsaturated compound into a saturated one*.



RING COMPOUNDS OF THE ALIPHATIC SERIES

The above relationship between saturated and unsaturated compounds shows that they all belong to the open chain series, *aliphatic compounds* or *open chain compounds*.

This holds rigidly true with the hydrocarbons and their simpler derivatives. In the case of certain derivatives which contain an anhydride group a different condition is sometimes met with in which the ends of the chain are joined and what was an open chain is converted into a *closed chain* or *ring* or *cycle*. The simplest case of this nature is the formation of lactones from *gamma*-hydroxy acids by loss of water (p. 242). It will be recalled that whenever an hydroxy or an amino acid which contains at least four carbon groups, with the hydroxy or amino group in the *gamma* or *delta* position, loses water the first carbon is brought into union with the fourth or fifth carbon through the oxygen atom or the NH group and a ring is thereby formed, **gamma-hydroxy butyric acid** yielding **butyro lactone** as follows:

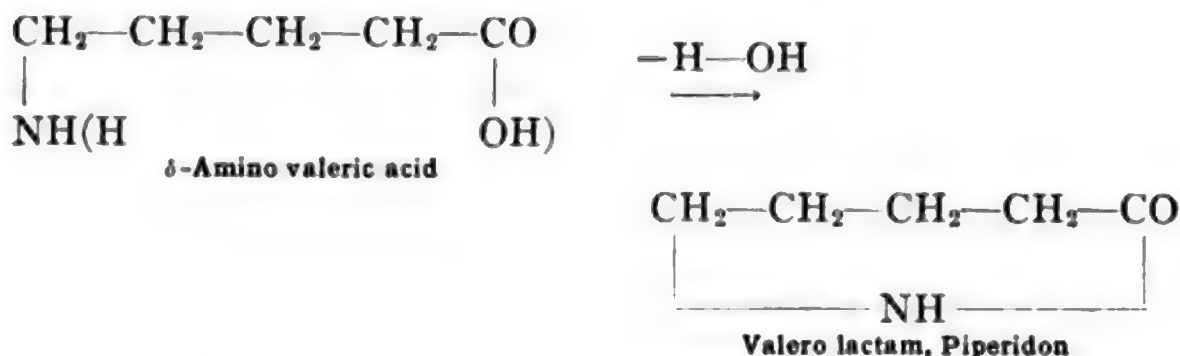


gamma-Amino butyric acid yields **pyrrolidon**, $\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CO}$

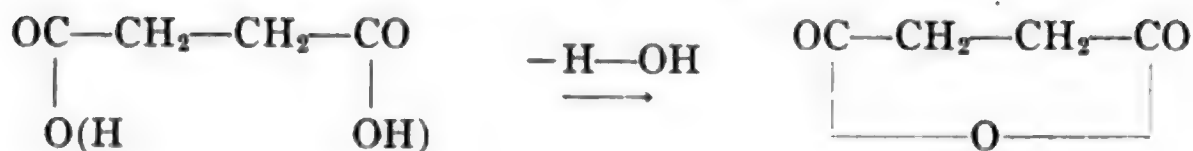
$$\begin{array}{c} | \\ \text{NH} \end{array}$$

(p. 851).

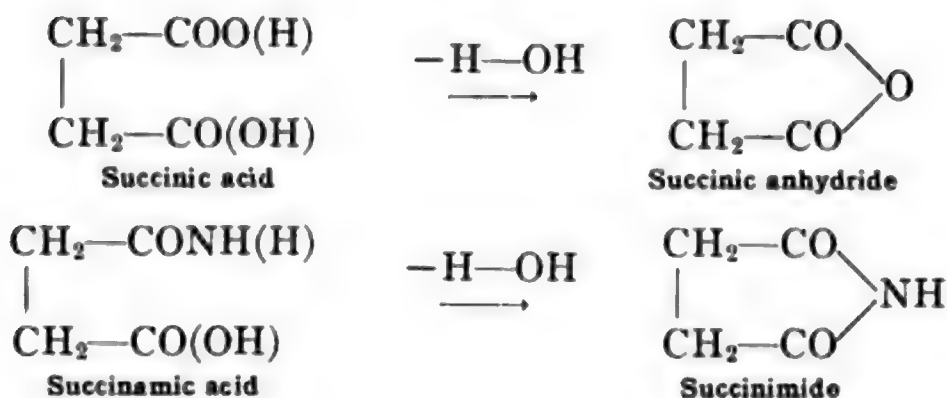
Similarly **delta-amino valeric** yields **valero lactam** or **piperidon** (p. 851).



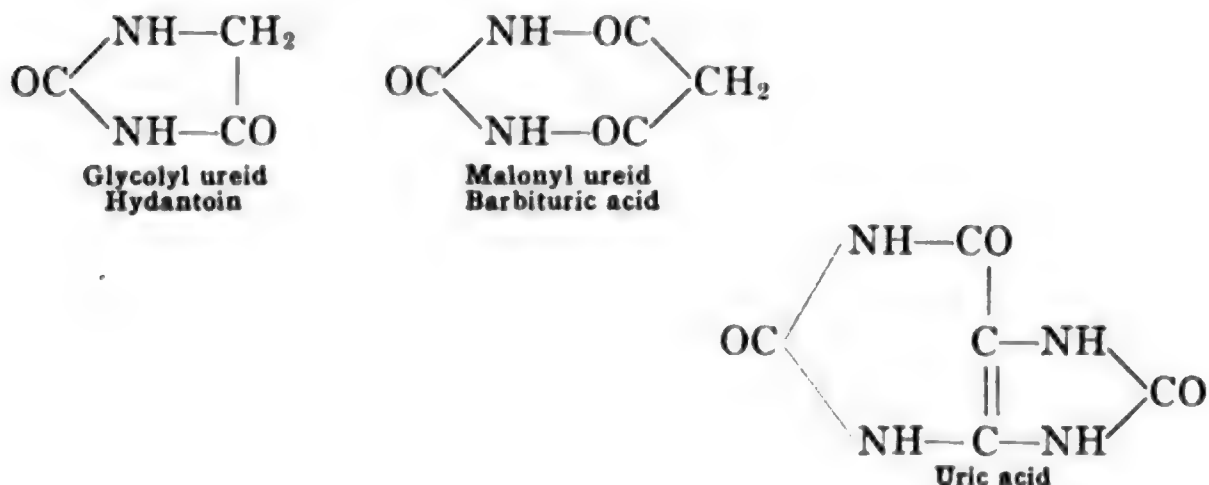
Another well known case is that of the formation of **succinic anhydride** from succinic acid, and of **succinimide** from **succinamic acid** (p. 280, 283).



or



The **ureids** and **uric acid** have also been explained by structural formulas of this ring type as follows:



The relationship of all of these compounds to definite open chain compounds has been thoroughly established, and the conversion of an open chain into a closed chain or ring is well understood. The formation of the ring results from the linking together, through an intervening non-carbon element or group, of the carbons which are at the ends of the chain or which are separated from each other by at least three intervening carbons or other groups. The uniting element or group in the compounds mentioned is either **oxygen** or the **imide** group, *i.e.*, an *anhydride* grouping, formed by the loss of water (H_2O), or ammonia (NH_3). Sulphur also acts as a link in similar ring compounds to be studied later.

Hetero-cyclic Compounds.—In no case, thus far cited, has a ring been formed which contains carbon groups *only*. Because of this fact, that the rings contain both *carbon* and *non-carbon* groups, they are termed *heterogeneous* rings and the compounds are known as *hetero-cyclic* compounds. While the hetero-cyclic compounds which we have given as illustrations are directly related to aliphatic or open chain compounds, and have been discussed in their proper place as members of the aliphatic series, there are other hetero-cyclic compounds which are either directly related to **benzene** or which can not well be considered until later. Therefore the hetero-cyclic compounds as a group will constitute the last main sub-division or section of our study.

We must, however, again recognize the fact that while it may seem natural to classify organic compounds so that all of those which have an open chain structure are in one class, and all of those which have a ring or cyclic structure are in another, yet no such exact separation or classification is practically possible.

Carbo-cyclic Compounds.—Contrasted with the hetero-cyclic compounds, which we have just been discussing in a general way, we have other compounds whose constitution is also that of a *closed ring* or *cycle*, but this ring is composed of *carbon groups only*. To such we assign the names *carbo-cyclic compounds* or *iso-cyclic compounds* and they embrace not only hydrocarbons but also all of the different groups of derivatives which we have heretofore studied.

Benzene.—By far the most important and most numerous of these carbo-cyclic compounds have as their mother substance the hydrocarbon **benzene**, and the names *Benzene Series*, *Benzene Compounds*, or *Benzene Derivatives* are commonly used as synonymous with *carbo-cyclic compounds*.¹ This has led to the usual classification of organic

¹ It is well to be careful at the beginning in regard to this word **benzene**. Unfortunately there is another substance which goes commercially by the name of **benzine**, and the English language does not allow of a distinction in pronunciation. The two substances are wholly different. **Benzene** is a definite chemical compound—an individual substance—while **benzine** is a mixture of several compounds, and is simply a commercial product. Benzene is obtained as a distillation product of crude petroleum, and goes also by the name of *petroleum ether*. The use of the word *benzol* in English is wholly inadvisable. In chemical terminology *ol* means a hydroxy compound, and benzene is a hydrocarbon. The word *benzol* is German and not English. In commercial usage *benzol* has become common English, and is frequently used, but care should be taken to distinguish between commercial or trade language and true English chemical words.

compounds into *aliphatic compounds* and *benzene compounds*. Such a classification should be understood in the light of the explanations and limitations which we have been considering. *In this text the main division and classification used is as follows:

Part I: *Aliphatic* or open chain compounds; including certain *hetero-cyclic* compounds directly related to them.

Part II: *Carbo-cyclic* compounds; including not only carbon ring compounds *derived from benzene, iso-cyclic*, but also carbon ring compounds not derived from benzene, *ali-cyclic*; in addition to these the *hetero-cyclic* compounds as a group.

SECTION I. CARBO-CYCLIC COMPOUNDS

A. ALI-CYCLIC COMPOUNDS OR CARBO-CYCLIC COMPOUNDS NOT DERIVED FROM BENZENE.

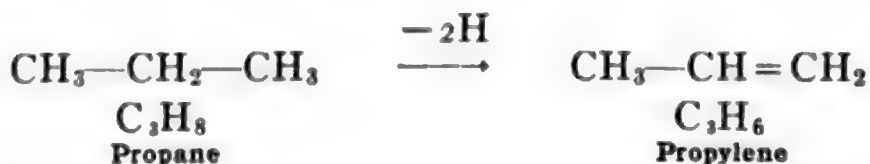
I. SATURATED ALI-CYCLIC COMPOUNDS

The hydrocarbons of the general formula C_nH_{2n} , the ethylene series, *e.g.*, **ethylene**, C_2H_4 or $CH_2 = CH_2$, are unsaturated compounds possessing the characteristic properties of such compounds, *viz.*, the property of forming addition products particularly with the halogen elements. Another group of hydrocarbons is known, however, the members of which possess the same general formula, but they do not form addition products, and therefore are not members of the unsaturated series. The compounds of this kind which are known are those containing three, four, five and six carbon atoms as follows:

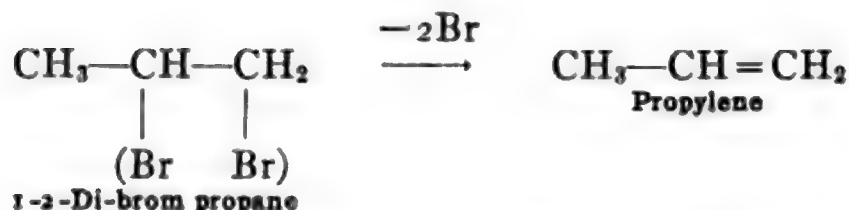
C_3H_6	Tri-methylene	or	Cyclo propane
C_4H_8	Tetra-methylene	or	Cyclo butane
C_5H_{10}	Penta-methylene	or	Cyclo pentane
C_6H_{12}	Hexa-methylene	or	Cyclo hexane

What are the properties of these compounds and what is their structure which can thus explain their isomerism with the olefines, and the fact that they are not unsaturated? The simplest member of the group, *viz.*, C_3H_6 , is known as **tri-methylene** or **cyclo propane**.

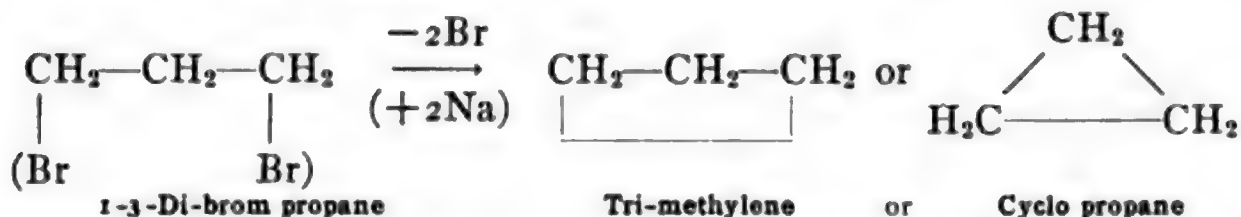
Tri-methylene, Cyclo Propane.—It is isomeric with **propylene** for which the structure has been shown to be $CH_3-CH=CH_2$. Now **propylene** is related to **propane** in that two hydrogen atoms in propane are lost from two adjacent carbon groups, the two carbons becoming doubly linked.



The result is accomplished by the loss of two bromine atoms from **1-2-di-brom propane** when it is heated with sodium.

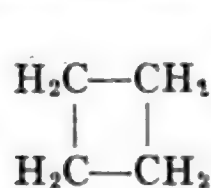


If instead of 1-2-di-brom propane we use 1-3-di-brom propane the product is **cyclo propane**.

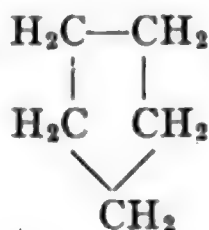


That is, instead of two adjacent carbons becoming doubly linked as in propylene, the two end carbons become linked together and the open chain compound is converted into a *closed chain* or *ring* exactly as in the lactones and lactams. The ring, however, has no intervening anhydride oxygen or *NH* group by which the end carbons are linked, but these are linked directly, thus giving a *carbo-cyclic* not a hetero-cyclic compound. The structural formula as given above agrees with the fact that **tri-methylene** is *not* an unsaturated compound though it has the general composition of the ethylene series. All of the valencies of the carbons are satisfied and there is no opportunity for the formation of addition products. As the compound contains *three* methylene groups it is known as **tri-methylene**, and as it is related to propane in that the open chain structure of the latter is converted into a ring or cycle it is known also as **cyclo propane**.

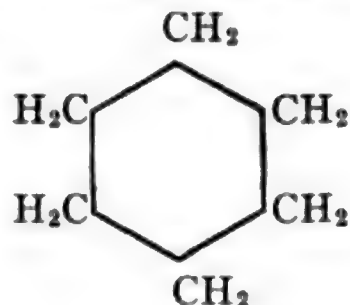
What we have said in regard to the compound C_3H_6 applies to the others mentioned, viz., C_4H_8 , C_5H_{10} and C_6H_{12} , which are the members of the homologous series. They are each prepared from the corresponding saturated homologue by reactions analogous to those given for tri-methylene. The structural formulas, as usually written, are:



C_4H_8
Tetra-methylene
Cyclo butane



C_5H_{10}
Penta-methylene
Cyclo pentane



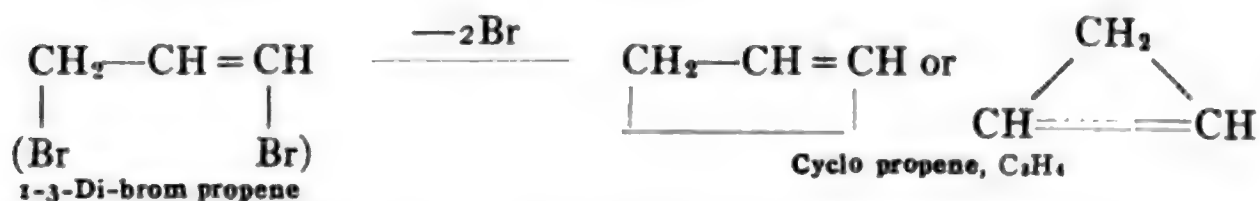
C_6H_{12}
Hexa-methylene
Cyclo hexane

Poly-methylenes, Cyclo Paraffins.—The names **tetra-methylene** or **cyclo butane**, **hexa-methylene** or **cyclo hexane**, etc., are analogous to **tri-methylene** or **cyclo propane**. For the homologous series the names **poly-methylenes** or **cyclo paraffins** are used.

Ali-cyclic Compounds.—Cyclo propane and its homologues, therefore, are *saturated carbo-cyclic compounds*. They are similar to aliphatic compounds in certain respects, and are not like benzene compounds. We indicate this by the name *ali-cyclic*, as suggested by **Bamberger**, to distinguish them from the *carbo-cyclic compounds* related to **benzene** which are termed *iso-cyclic*.

2. UNSATURATED ALI-CYCLIC COMPOUNDS

Another group of ali-cyclic compounds should be mentioned briefly, viz., those which contain unsaturated groups, *i.e.*, carbon atoms linked by double or triple bonds. Just as **1-3-di-brom propane** yields *cyclo* propane or **tri-methylene** so **1-3-di-brom propene** yields a cyclic compound in which a double bond is present.



Compounds containing a triple linking are also known and are prepared by similar reactions.

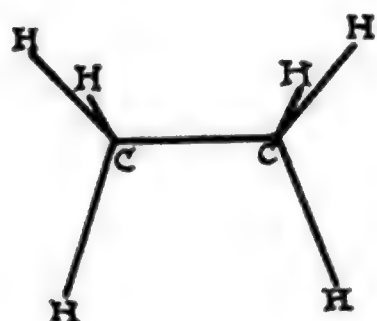


All of these ali-cyclic compounds containing double or triple bonds are unsaturated compounds distinctly different from the saturated ali-cyclic compounds.

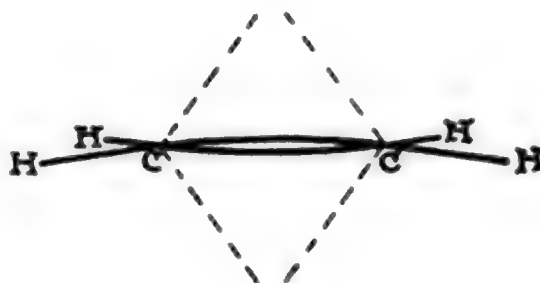
Strain Theory of Carbo-cyclic Compounds

Referring again to the saturated ali-cyclic, or poly-methylene, compounds and comparing them with the isomeric olefine compounds, we find some exceedingly interesting facts. In connection with the idea

that carbon is a tetravalent element, and that in organic compounds it may best be represented in space as situated at the center of a regular tetrahedron, with its four lines of affinity or valence equilaterally and equiangularly distributed, we find that the conversion of an open chain compound into a closed chain or ring compound brings out some very important points which agree with known facts, and which lead to the explanation of important relationships. As was explained in connection with the olefine hydrocarbons, the double bond existing between two carbon atoms is a point of weakness rather than strength. This is indicated by the fact that compounds containing such doubly or triply linked carbon atoms readily break one of the double bonds, and form addition products which are saturated compounds. The probable explanation of this weakness is, that according to the tetrahedral or space formulas, when two carbon atoms are doubly or triply linked the lines of affinity or union are subject to a considerable strain, while two carbon atoms singly linked are under no strain. This will be seen from the following drawings and still better if the tetrahedral models are examined.



Ethane
 $\text{H}_3\text{C}-\text{CH}_3$



Ethylene
 $\text{H}_2\text{C}=\text{CH}_2$

FIG. 7.

If now, by the reactions which we have discussed, we convert derivatives of the saturated open chain compounds into carbo-cyclic compounds, a strain is produced in the formation of the ring just as there is in the formation of ethylene.

The poly-methylene compounds may be represented by the following drawings:

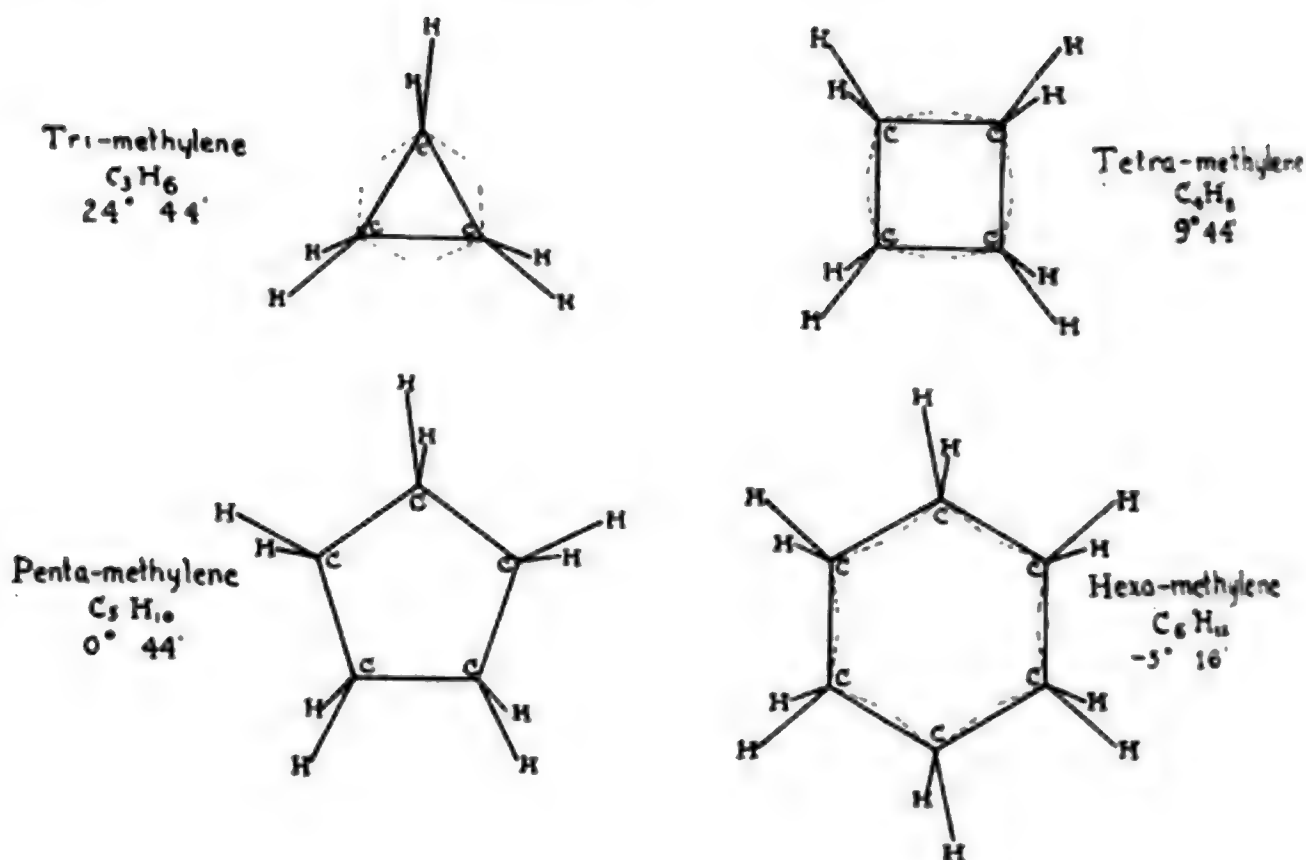


FIG. 8.

According to the tetrahedral theory the four valencies of carbon are represented by the four axes of the regular tetrahedron. The angle between any two of these axes amounts to $109^\circ 28'$. In the above drawings the light dotted lines represent this normal angular difference between two of the carbon valencies. The heavy full lines linking the carbons together show the position which these axes or lines of union must assume in the formation of a symmetrical cyclic compound of three, four, five or six carbons. The amount in degrees and minutes which is given with each formula is the angular distance through which each of the linking bonds must be moved from the normal in order to form a symmetrical cycle of the carbons. This angular distance represents the *strain* under which the cyclic compound exists. It will be noticed that the strain decreases as we pass from tri-methylene to tetra-methylene and to penta-methylene and that it then increases, but in the opposite direction, as we pass to hexa-methylene. In the case of penta-methylene this angular difference is so small that it can not be shown in the drawing and therefore only one set of lines appears.

From these figures, which are the result of mathematical calculation, we see that the carbo-cyclic compounds which should be the most

stable are those containing *five* carbon atoms in the ring, as in penta-methylene, in which the strain amounts to only $0^{\circ} 44'$. This is found to be the fact for penta-methylene is more stable than hexa-methylene, tetra-methylene or tri-methylene. It may be mentioned also that ali-cyclic compounds of more than eight carbons in the ring have never been prepared.

While, however, penta-methylene is the most stable ali-cyclic compound of the poly-methylene group it is **hexa-methylene** which is of special interest and importance. This importance is due to the fact that it is the connecting link between the ali-cyclic compounds (carbocyclic compounds not derived from benzene, *i.e.*, the poly methylenes) and benzene itself. Thus it becomes the connecting link between the aliphatic open-chain compounds and the very large and important division including benzene and its derivatives.

B. CARBO-CYCLIC COMPOUNDS DERIVED FROM BENZENE, ISO-CYCLIC COMPOUNDS OR AROMATIC COMPOUNDS

1. BENZENE SERIES

A. HYDROCARBONS

CONSTITUTION OF BENZENE

Aromatic Compounds.—The carbo-cyclic compounds which in number far exceed those of the aliphatic series were originally called *aromatic compounds* because many of them possess aromatic properties, *e.g.*, oil of wintergreen, oil of bitter almonds, etc. They were included with the paraffin compounds in the various groups of alcohols, aldehydes, acids, etc. Later it was found that they differed from the aliphatic compounds and finally it was shown that the hydrocarbon **benzene** is related to the aromatic compounds just as **methane** is to the aliphatic compounds, *i.e.*, as the mother substance.

Benzene Series.—This gave rise to the use of the names *benzene series* and *benzene compounds* in place of the name *aromatic compounds*. As many of the compounds since discovered and belonging to this series are not aromatic the former names are better as all of them are related to benzene. Strictly speaking, however, the benzene series proper does not include all of the carbo-cyclic compounds related to benzene and which are included in the terms *iso-cyclic* or *aromatic* as distinct from *aliphatic*, *e.g.*, **naphthalene**, etc. Generally speaking, however, the names are used synonymously.

Benzene.—What then is **benzene**, the mother substance of this large division of organic compounds which as we shall find are unsurpassed in their application to the industries and to daily life? When coal gas is made by the destructive distillation of coal the products in the first place are probably **water**, **methane** and **ammonia**. These being subjected to considerable heat result in the formation of numerous more complicated compounds. The gaseous products, consisting of **methane**, **hydrogen**, etc., constitute crude illuminating gas. The solid

residue is *coke*. The liquid products consist of two parts: water, containing principally **ammonia** gas in solution, and a thick tarry liquid known as *coal tar*, which separates largely from the water.

Coal Tar.—This coal tar is the crude source of many compounds of the *benzene series*. On redistillation of the coal tar numerous fractional distillates are obtained from which different compounds are isolated, (p. 497).

Light Oil.—The first distillate which comes over below 170° is known as *light oil*, because it floats on water. Most of the benzene itself is obtained by further fractionation of this light oil.

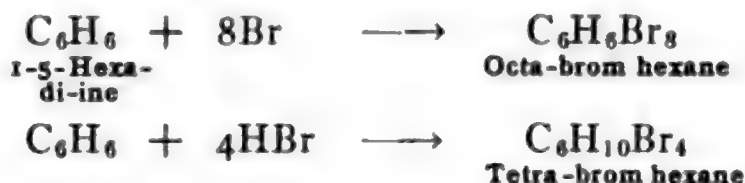
C_6H_6 , C_nH_{2n-6} .—By analysis and molecular weight determination the formula for benzene has been shown to be C_6H_6 . What are the properties of this compound and how may its structural formula be represented? The formula C_6H_6 corresponds to the general formula C_nH_{2n-6} which would indicate an unsaturated hydrocarbon.

Di-propargyl.—Now we have previously described an unsaturated hydrocarbon of this composition, viz., **di-propargyl** or **1-5-hexa-di-ine** (p. 163). It was shown to be a derivative of hexane containing two triple bonds or acetylene groups. The structural formula as indicated by its systematic name is:



Benzene, however, is an entirely different compound than this, *i.e.*, it is isomeric with di-propargyl. It does not act like an unsaturated compound and, therefore, can not be represented by a structural formula like the above. Some of the characteristic differences between these two isomeric compounds are shown by the following reactions.

Like other unsaturated compounds **di-propargyl** readily forms addition products taking up *eight atoms* of bromine or *four molecules* of hydrobromic acid being converted thereby into bromine substitution products of the saturated hydrocarbon **hexane**.



Benzene and Bromine.—Benzene, however, does not act in this way with bromine nor at all with hydrobromic acid. When bromine acts on benzene the product usually formed is a substitution product,

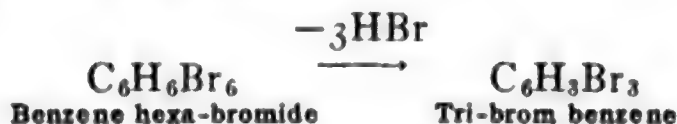
e.g., **monobrom benzene** in which a hydrogen is substituted by bromine.



If, however, the reaction takes place in the sunlight an addition product is formed; but, instead of *eight* bromine atoms being added, as in the case of hexa-di-ine, *only six* bromine atoms are taken up by the benzene.



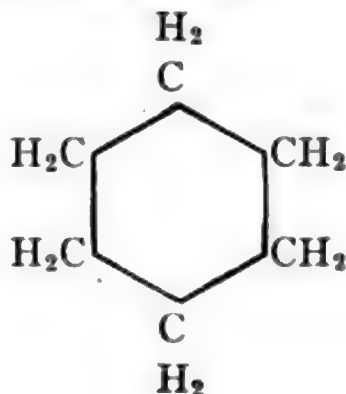
According to our ideas of saturation this compound is still unsaturated as it corresponds to the general formula of the olefines, viz., C_nH_{2n} . This hexa-brom addition product of benzene does not act like an unsaturated compound. In contrast to such properties it readily decomposes losing 3HBr , and becomes converted into a *tri-brom substitution* product of benzene.



Hexa-hydro Benzene.—Similar to the bromine addition product is the hydrogen addition product. Six hydrogen atoms can be added to benzene, but *only six* as in the case of bromine.



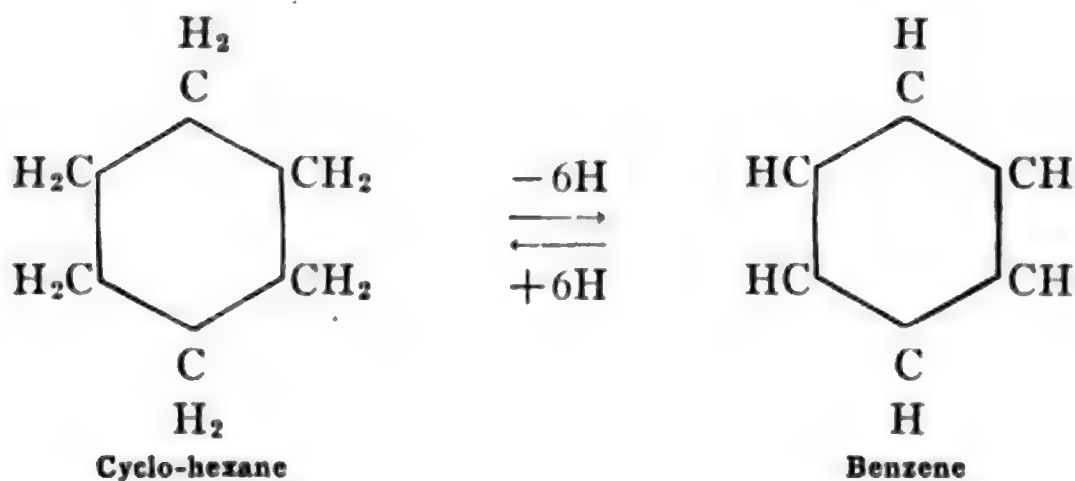
Cyclo-hexane.—The resulting compound C_6H_{12} corresponds to the olefine unsaturated hydrocarbons, C_nH_{2n} , and is isomeric with hexene. **Hexene**, however, readily adds two atoms of hydrogen and yields **hexane**, whereas **hexa-hydro benzene** is with difficulty converted into **hexane**. The compound, therefore, is not unsaturated. More important still is the fact that it proves to be *identical* with **hexa-methylene** or **cyclo-hexane** which, as we have recently shown, is a carbocyclic compound represented as follows:



Thus the addition product formed by adding six hydrogens to benzene is a compound which we represent as six methylene groups linked together in a ring.

Hexagon Formula.—If in hexa-methylene the six methylene groups are symmetrically arranged we shall have a structural formula represented by a hexagon, as this geometric figure is symmetrical and of six points and six sides. This has been already shown on page 464.

The relationship between **benzene** and **cyclo-hexane** may, therefore, be represented as follows:



Such a formula as this agrees with the facts we have thus far given in regard to benzene, viz., that it is not an unsaturated open chain compound, nor is it an ali-cyclic compound like cyclo-hexane. It is, however, directly related to the latter.

Properties.—What are other properties of this compound benzene, and how can its constitution be explained in accord with these properties, and does the formula just suggested, because of its relationship to cyclo-hexane, fit the case?

In the first place, as already stated, when benzene is treated with bromine, substitution products are more readily formed than addition products, and the former are the stable compounds. While methane, because of its saturated character, does not form addition products, but only substitution products, benzene forms both, but the substitution products are the more stable. Evidently benzene is more like a saturated compound than an unsaturated one in spite of the fact that it has eight less hydrogen atoms than are sufficient to satisfy the six carbon atoms according to the open-chain structure, and six less than sufficient according to the cyclo-paraffin structure.

Substitution Products.--The substitution products of benzene, as will be explained again later on, are wholly analogous to those of the paraffin hydrocarbons, and may be simply illustrated as follows:

C_6H_5-Cl ,	Mono-chlor-benzene
$C_6H_4=Br_2$,	Di-brom-benzene
C_6H_5-OH ,	Hydroxy benzene
$C_6H_5-NH_2$,	Amino benzene
$C_6H_5-CH_3$,	Methyl benzene

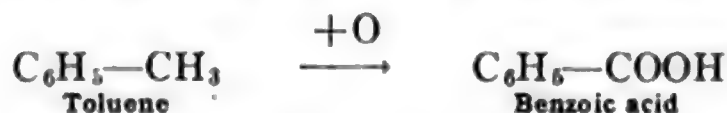
The last compound, viz., methyl benzene, is the first of the homologous series of benzene hydrocarbons just as methyl methane is the first homologue above methane.

Considering now benzene and its relation to these substitution products we find certain facts which differentiate it from the paraffin hydrocarbons, and which also enable us to devise a satisfactory structural formula.

Nitro Products.—(a) Benzene and its homologous hydrocarbons readily form *nitro-substitution products* when treated with nitric acid, whereas the paraffin hydrocarbons form nitro-substitution products only indirectly, $C_6H_5-NO_2$, **nitro benzene**.

Sulphonic Acids.—(b) The same is true in regard to the reaction of the benzene hydrocarbons with sulphuric acid. Substitution products are formed directly, and are known as *sulphonic acids*, $C_6H_5-SO_2OH$, **benzene sulphonic acid**.

Homologues Oxidized.—(c) The homologues of benzene, e.g., methyl benzene or **toluene**, $C_6H_5-CH_3$, are very easily oxidized, and the *methyl group*, CH_3 , is converted into the *carboxyl group*, $COOH$. This reaction takes place with difficulty in the case of the paraffins.



Halogen Products.—(d) The halogen substitution products of benzene are less active than the corresponding products in the paraffin series.

Hydroxyl Products.—(e) The hydroxyl substitution products of the benzene hydrocarbons are more strongly *acid* than the hydroxy paraffins, i.e., the alcohols. This means that the radical (C_6H_5-) is more acid than the radical (CH_3-).

Thus we see that in these several ways the benzene hydrocarbons differ from their aliphatic relatives. The preceding facts together with those regarding isomerism, which we shall now discuss, show the most striking properties of the benzene compounds, and when considered in connection with the relationship of benzene to cyclo hexane, lead to the most probable theory in regard to the structure of benzene itself and of all of its derivatives.

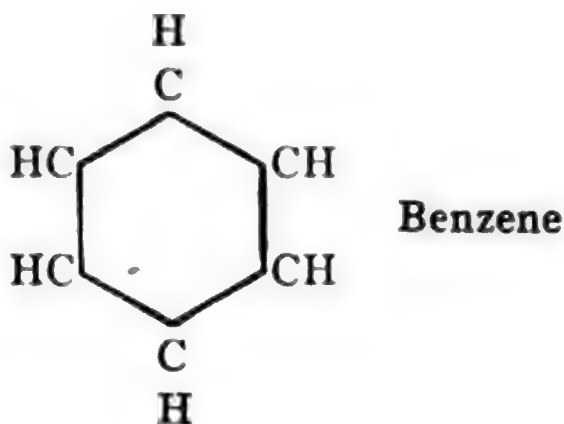
Isomerism

A study of the isomeric substitution products of benzene reveals some striking facts which furnish the strongest support for the accepted structural formula.

One Mono-substitution Product.—If benzene were an open chain unsaturated compound similar to 1-5-hexa-di-ine we should have, as in the case of the latter and other like compounds, several isomeric mono-substitution products. *But* benzene yields only *one* mono-substitution product of any type. This can mean only one thing, viz., that in benzene *all six of the hydrogen atoms are alike*.

Symmetry of Benzene.—If then benzene is a carbo-cyclic compound, as is so strongly indicated by its relationship to cyclo-hexane, the structural formula should express first of all this equivalence or likeness of the hydrogen atoms. In any geometric representation of such a condition we would naturally indicate it by a symmetrical figure.

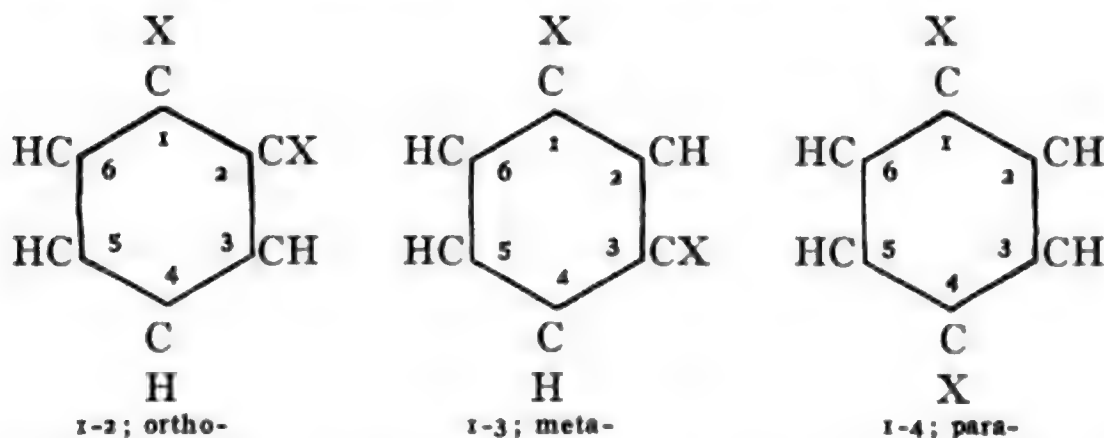
Hexagon Formula.—The hexagonal arrangement of six carbon atoms, each one of which holds in combination one hydrogen atom, gives us such a symmetrical structure for a compound whose composition is C_6H_6 . Represented in its simplest form and as indicated by its relation to cyclo-hexane we have



In this formula all of the hydrogen atoms are represented as similarly placed in reference to each other. Before enlarging upon this formula and showing its complete form let us see if it agrees with the facts in regard to isomerism. Its agreement with the fact that only one mono-substitution product is known has just been considered. How is it in regard to the poly-substitution products? The facts are these:

Three Isomeric Di-substitution Products.—There are known *three* and *only three* isomeric *di-substitution products* of benzene and also *three* and *only three* isomeric *tri-substitution products*. All of the three possible isomeric compounds are definitely known in so many cases that the above statement is considered as universally true.

Three Isomeric Tri-substitution Products.—If we examine the hexagon formula we find that *three and only three* isomeric substitution products are possible in both instances, where two and where three substituting elements are present. As in the hexagon formula all of the hydrogens are alike, the only different arrangements conceivable for *two* substituting elements or groups are the following:



The difference in these compounds must be due to the relative positions of the two carbon groups in which the substitution has occurred.

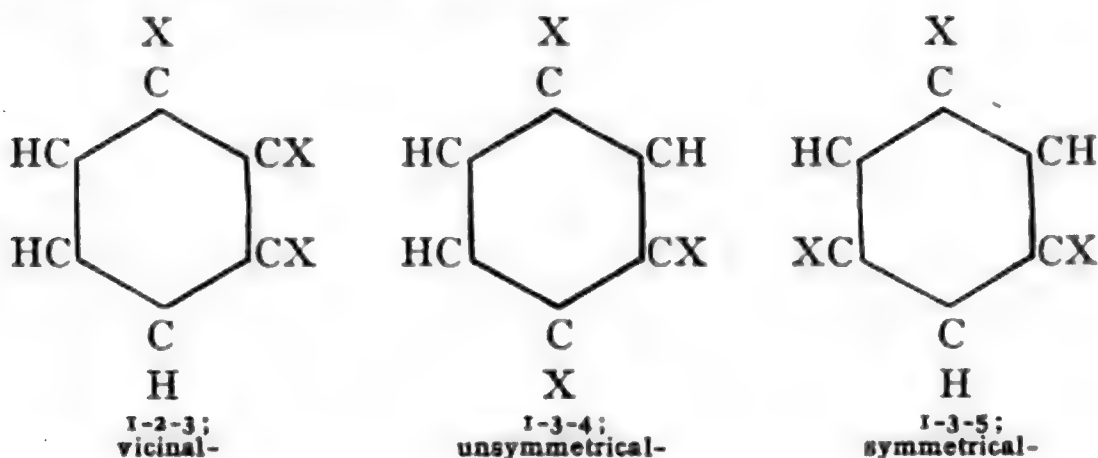
Ortho.—Any compound formed by the substitution of two elements in any two positions that are next to each other must be exactly the same. That is, the positions 1-2, 1-6, 2-3, 3-4, 4-5, 5-6 are all alike because of the symmetry of our formula, and the likeness of all of the hydrogen atoms. Such a compound is known as an *ortho* compound.

Meta.—In the same way positions 1-3, 1-5, 2-4, 2-6, 3-5, 4-6 are all alike and only one di-substitution product is possible where the substitution is in carbon groups separated from each other by one intervening carbon. A compound of this type is known as a *meta* compound.

Para.—Finally the third arrangement is the only new form conceivable as positions 1-4, 2-5, 3-6 are all alike. In this type the substituting groups are removed from each other by two intervening carbons, or they are directly opposite each other in the hexagon ring. Such a compound is known as a *para* compound. Therefore the possibilities of the theory of the hexagonal formula for benzene are that three and only three di-substitution products of benzene are conceivable, and this is in agreement with the *fact* that three and only three are known.

With the same clearness we can show that *three and only three* tri-substitution products of benzene being known, is in agreement with our theory by which three and only three are possible. The possible isomeric tri-substitution products are shown as follows:

Vicinal, Unsymmetrical, Symmetrical.

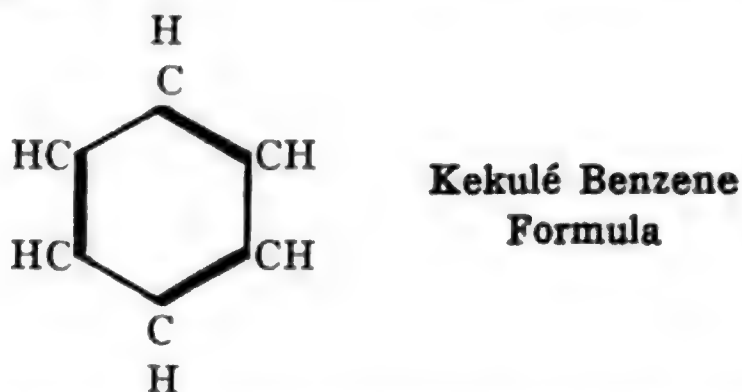


Examination will confirm the statement that these three are the only different arrangements possible for 1-2-3, 1-6-5 and 2-3-4 are alike; 1-3-4, 1-5-4, 1-2-4 and 2-3-5 are alike; 1-3-5 and 2-4-6 are alike, and any other arrangement that can be figured out will prove to be identical with one of these three. Therefore here again the theory is in agreement with the facts. Not only then is there agreement between theory and fact in regard to the relationship of benzene to cyclo-hexane, but there is like agreement in fact and theory in connection with isomerism in the case of poly-substitution products and absence of isomerism in mono-substitution products.

Position Isomerism.—This type of isomerism is plainly structural isomerism, but to characterize it further it is termed *place* or *position isomerism*.

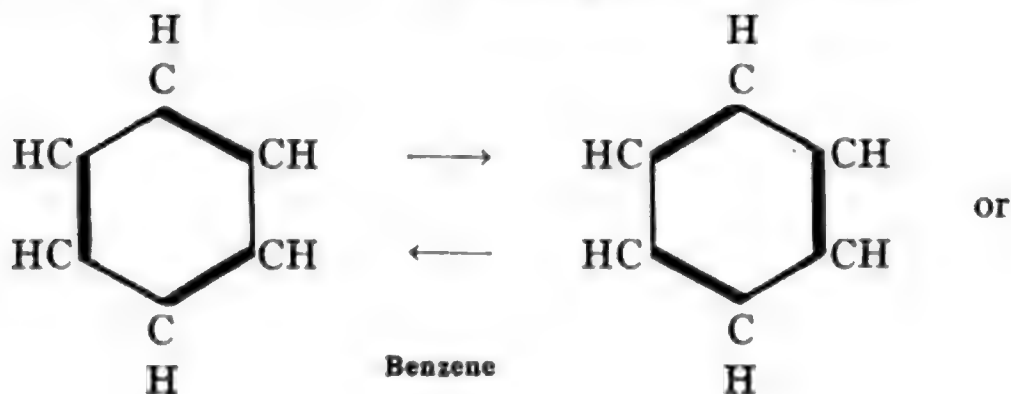
Hexagon Theory and Tetra-valence of Carbon.—One point, however, and that a fundamental one, we have not yet considered. Does

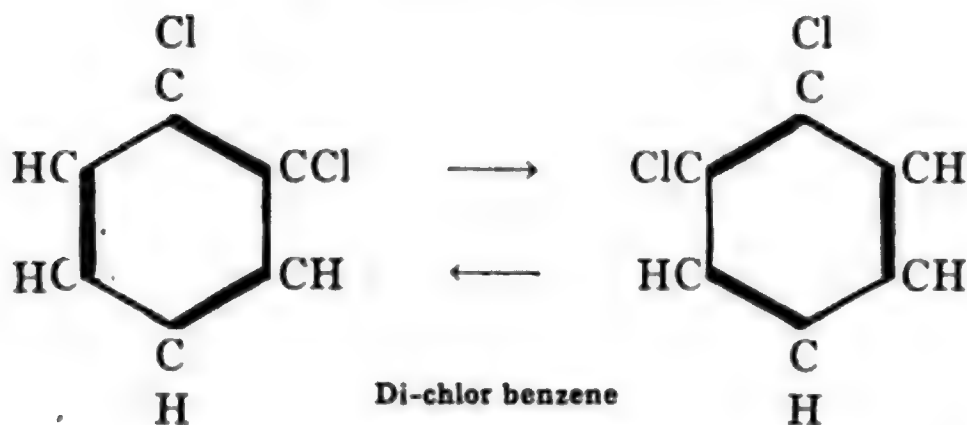
the theory of the hexagon formula for benzene agree with the *tetra-valence of carbon*, the idea so fundamental in connection with organic compounds? Plainly, again, the formula as we have given it thus far does not agree with the conception that carbon is tetra-valent, for only three valencies for each carbon are represented in the formula. To expand the simple hexagonal formula to agree with the idea of the tetra-valence of carbon it has been necessary to introduce double bonds alternately into the hexagon ring formula, thus representing each carbon with four bonds as follows:



Kekulé Formula.—This formula, as above represented, was devised by **August Kekulé** in 1865 and therefore is known and spoken of as the **Kekulé Formula** or the **Kekulé Theory**, also as the *hexagon formula* and as the *benzene ring*.

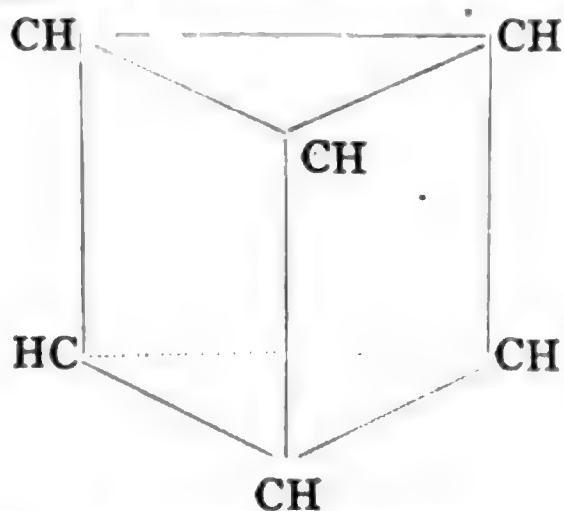
Oscillation Theory.—Careful consideration, however, will show that the di-substitution products 1-2 and 1-6 are not exactly the same for in one case (1-2) the carbon groups holding the substituting elements are linked by double bonds, whereas in the other case (1-6) they are singly linked. To overcome this **Kekulé** claimed that, in such an arrangement in space, oscillation takes place so that at one instant the structure is as represented, and in the next the double bonds change position so that the image form of the formula is in existence, oscillation from one to the other form taking place continually.





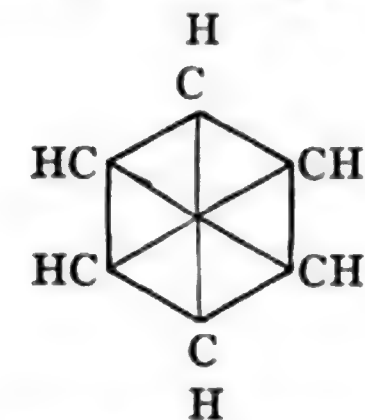
Facts that have been brought to light since the suggestions of Kekulé, in the study of *tautomerism* and *desmotropism*, give strong support to this oscillation theory.

Ladenburg Formula.—Ladenburg, however, not satisfied with Kekulé's formula suggested another known as the *prism formula*.

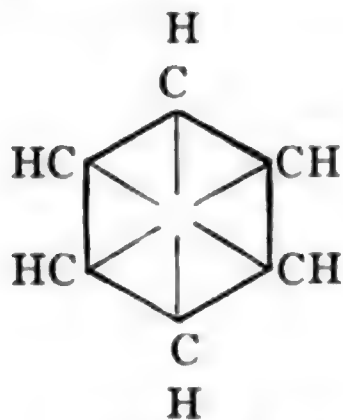


Ladenburg, Prism Formula

Claus, Armstrong and Baeyer.—Still other formulas have been suggested on account of this difficulty, each endeavoring to avoid the necessity of oscillation in order to satisfy the four valencies of carbon. One of these was suggested by **Claus** and called the *diagonal formula*; and another by **Armstrong and Baeyer** and known as the *centric formula*.



Claus, Diagonal Formula
for Benzene



Armstrong and Baeyer,
Centric Formula
for Benzene

It is not desirable in this place to discuss at greater length these other formulas, but simply to mention them together with the names of the men who have suggested them. All of these men were chemists who did much to establish our ideas in relation to the constitution of benzene and its structural representation in agreement with known facts. After all of these various suggestions and the discussions which they brought forth Kekulé's original complete formula still remains as the best representation of the structure of this important compound, and is the one universally accepted.

Benzene Hexagon in Space.—One more idea should be referred to in connection with the Kekulé theory. The Kekulé formula as we write it represents, of course, no space relations, but is simply a flat or plane representation of his idea. In accordance with the theory of van't Hoff and LeBel, carbon is represented as situated at the center of a regular tetrahedron, and the benzene ring of Kekulé becomes, therefore, a ring or hexagon composed of six such tetrahedrons. Such a formula will have the space arrangement as given for hexa-methylene (p. 464). In these poly-methylene or cyclo-paraffin compounds it will be recalled the **penta** and **hexa** carbon rings have the least strain, the former $0^{\circ} 44'$ and the latter $-5^{\circ} 16'$, and are consequently the most stable.

After thus considering the theoretical basis for the constitution of benzene, as it is borne out by facts demonstrated in the laboratory, we shall now turn to a consideration of the individual compounds of the series and their relation to each other. We shall begin, as in the aliphatic series, with the hydrocarbons.

Homologous Series, C_nH_{2n-6} .—The homologous series of the benzene hydrocarbons showing the more important and common members is as follows:

C_6H_6	Benzene.
C_7H_8	Toluene.
C_8H_{10}	Xylenes. .
C_9H_{12}	Mesitylene, etc.
$C_{10}H_{14}$	Cymene, etc.
$C_{11}H_{16}$	Penta-methyl benzene, etc.
$C_{12}H_{18}$	Hexa-methyl benzene.
$C_{13}H_{20}$	Heptyl benzene.
$C_{14}H_{22}$	Octyl benzene.
$C_{16}H_{26}$	Penta-ethyl benzene.

- $C_{18}H_{30}$ Hexa-ethyl benzene.
 $C_{22}H_{38}$ Hexa-decyl benzene.
 $C_{34}H_{42}$ Octa-decyl benzene.
 $C_{28}H_{44}$ Tri-methyl hexa-decyl benzene.

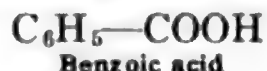
It will be noted that there are not as many known members of this homologous series of benzene hydrocarbons as there are of the methane series (p. 19). There is the same constant difference in composition between the successive members of this series as we found in the case of the methane series, viz., CH_2 , and we shall find that this is due to the same fact, viz., that in converting any hydrocarbon into the next higher member the *methyl* radical is substituted in place of hydrogen.

Benzene, C_6H_6

Coal Tar.—Benzene occurs in coal tar which is a heavy liquid obtained as a distillation product when coal is heated for the purpose of making coal gas or coke.

It was discovered in 1825 by Faraday in a liquid obtained by compressing oil gas made from shale or bituminous coal, and in 1845 Hofmann found it in coal tar. It is obtained from the fraction of coal tar distillate, boiling at 80° – 110° . It boils at 79° and melts at 5.4° . Its specific gravity is 0.90 (0°). It is a colorless, light, mobile liquid that burns readily in the air with a smoky flame due to its large amount of carbon.

Preparation from Benzoic Acid.—Benzene may be prepared from its compounds by a reaction similar to that used in preparing methane from acetic acid. **Benzoic acid** bears the same relation to benzene that acetic acid does to methane, viz., a mono-carboxyl substitution product.



Benzene may, therefore, be made by distilling a mixture of benzoic acid and lime just as methane is made by distilling a mixture of acetic acid (or sodium acetate) and lime.

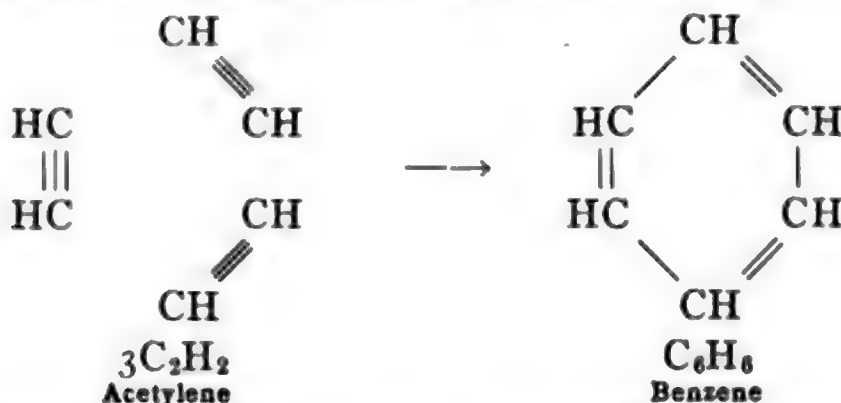


Synthesis of Benzene and Homologues.—There are other methods of preparing benzene and its homologues which show their relation to the aliphatic series. We have already dwelt upon the relationship between benzene and cyclo-hexane, showing that benzene is dehydrogenated cyclo-hexane.

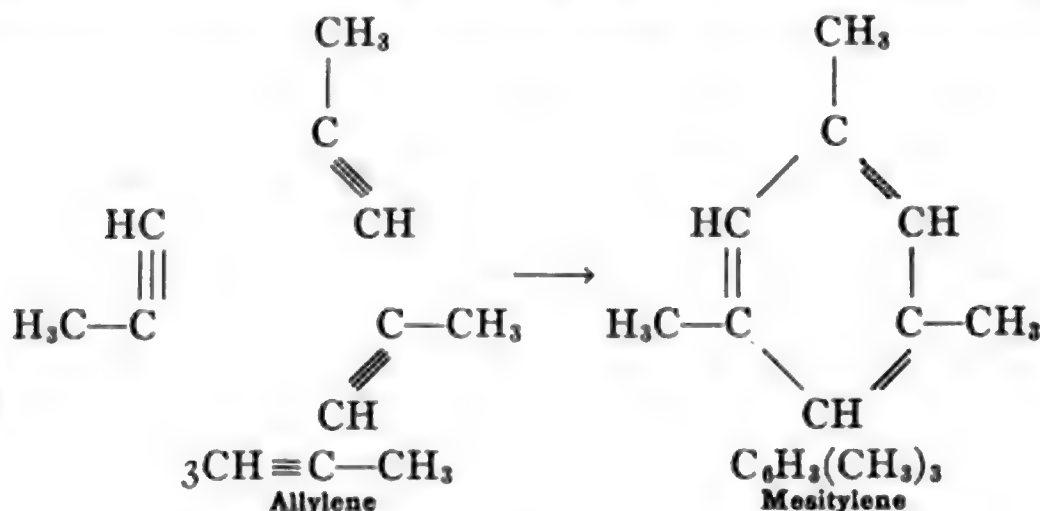
Benzene from Acetylene.—Benzene may be prepared directly from one of the unsaturated open chain compounds, viz., from **acetylene**, $\text{CH}\equiv\text{CH}$. When this hydrocarbon is passed through a red hot tube it is simply broken down into its elements. If, however, it is heated more slowly, it polymerizes and benzene is obtained.



Such a polymerization may be represented in the following manner in agreement with ideas in regard to both acetylene and benzene.



Mesitylene from Allylene.—In a similar way **methyl acetylene** or **allylene** polymerizes and yields **mesitylene** which is **tri-methyl benzene**.



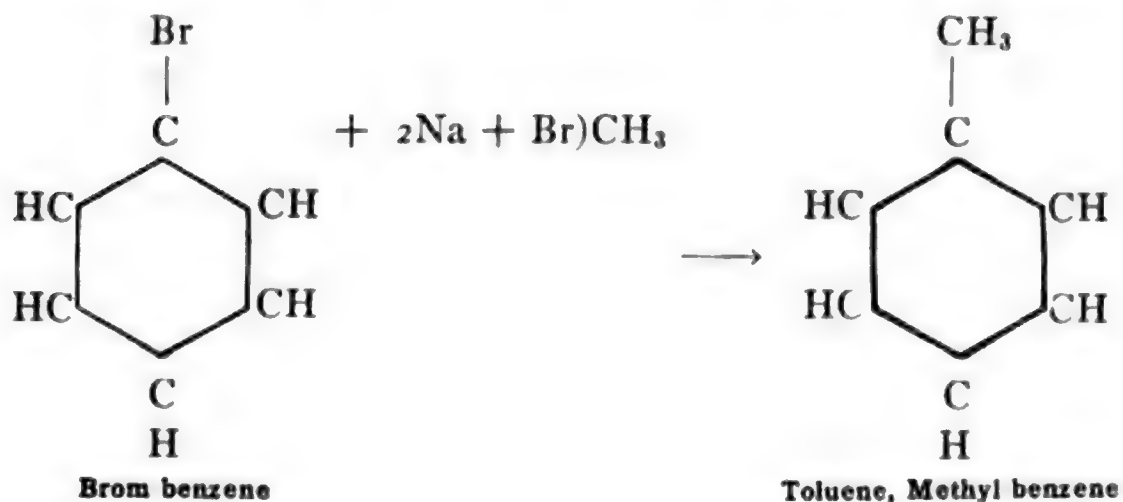
These two syntheses are of especial importance as showing the direct relationship between the hydrocarbons of the aliphatic series and the hydrocarbons of the benzene series.

Toluene, $C_6H_5-CH_3$

Toluene occurs naturally in the *balsam of tolu*, hence its name. It occurs also in coal tar, along with benzene. It is found mostly in the fraction of coal tar distillate boiling at $110^\circ-140^\circ$.

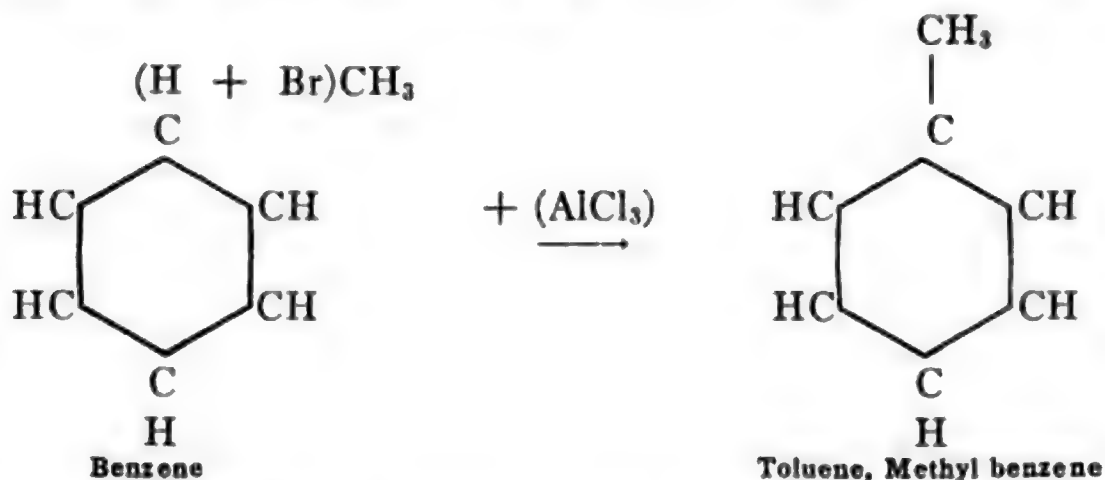
Fittig's Synthesis.—When Kekulé brought out his benzene theory the relation between toluene and benzene, the first two members of the homologous series of benzene hydrocarbons, was not known. It was worked out by **Fittig** and **Tollens** by means of what is known as the **Fittig synthesis**, which is based on a reaction exactly analogous to the **Wurtz reaction** for the synthesis of the homologous members of the aliphatic series of hydrocarbons.

When a halogen substitution product of benzene, *e.g.* **brom benzene**, is treated with a methyl halide and metallic sodium, toluene is obtained. This proves that **toluene** is **methyl benzene**.



Fittig first called the product of this reaction methyl benzene, and did not know that it was toluene. When, however, the identity of this substance with toluene was proven it cleared up at once the relationship between the first two members of the homologous series of benzene hydrocarbons and later of the entire series.

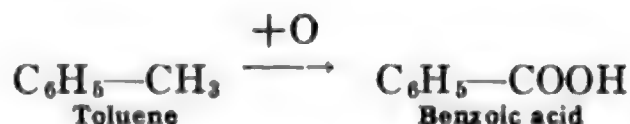
Friedel-Craft Reaction.—Another synthetic reaction of great importance in preparing the homologues of benzene is the **Friedel-Craft reaction**. When a hydrocarbon is treated with a *methyl halide* in the presence of **aluminium chloride** the methyl group is substituted in the hydrocarbon.



Toluene is similar to benzene in its general appearance. It is a colorless, light, mobile liquid boiling at 110° , and with specific gravity of 0.88 (0°). In its chemical properties toluene is distinctly different from benzene.

Ease of Substitution.—The substitution products of toluene are much more readily formed than similar ones in the case of benzene. The presence of a methyl group substituted in the benzene ring seems to make the compound more easily susceptible to further substitution in the ring itself.

Oxidation.—Oxidizing agents which attack benzene with difficulty react readily with toluene, and the substituted methyl radical becomes oxidized to carboxyl.

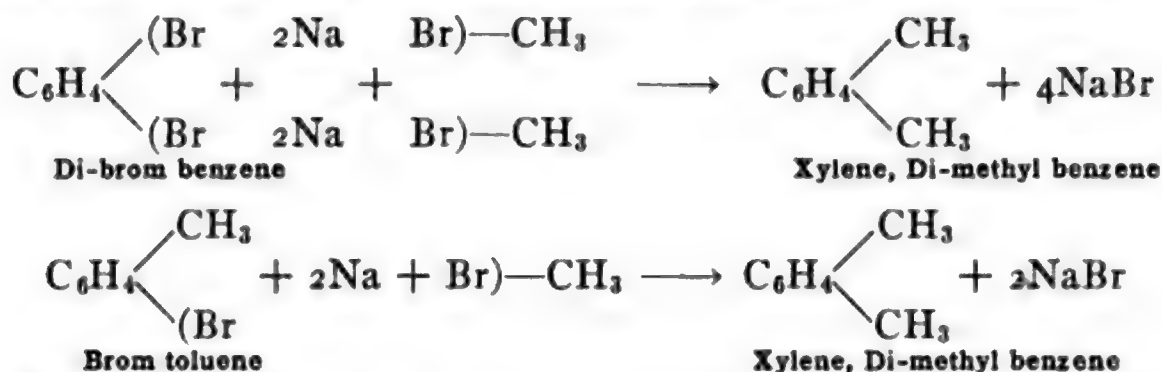


This oxidation of the methyl radical to carboxyl emphasizes a difference between benzene compounds and aliphatic compounds for in the latter, it will be recalled, the direct oxidation of a methyl group to a carboxyl group is impossible. Only one toluene is known which agrees with the theory as only one mono-methyl benzene is possible.



Isomeric Xylenes.—Xylene has been shown to have the constitution of **di-methyl benzene**, but as we should expect, being a di-substituted benzene three isomeric hydrocarbons are known all of which

have this constitution. This constitution has been proven by means of **Fittig's synthesis** from **di-brom benzene** and from **brom toluene**.

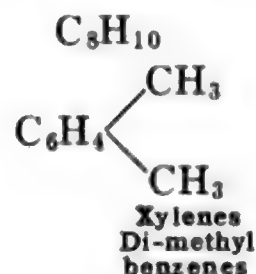
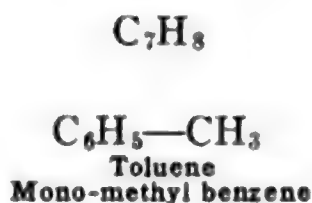
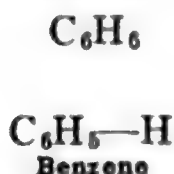
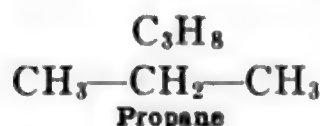
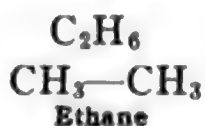
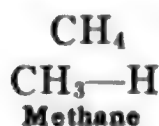


Ethyl Benzene.—By the same synthesis another hydrocarbon has been made from **mono-brom benzene** and ethyl bromide which has the empirical formula C_8H_{10} , but which must be **mono-ethyl benzene**.

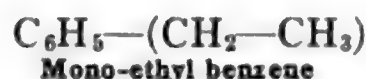


These two compounds **di-methyl benzene** and **mono-ethyl benzene** are simple structural isomers, while the three **di-methyl benzenes** are place isomers.

These hydrocarbons together with toluene clearly illustrate the fact that the homologous members of the benzene series of hydrocarbons bear exactly the same relationship to each other as do the homologous members of the aliphatic series of hydrocarbons. The homology in both cases is due to the same fact, viz., that the methyl radical is substituted for a hydrogen of a hydrocarbon in making the homologous hydrocarbon next higher up, *i.e.* containing one more carbon atom. The composition of the homologues changes by the quantity CH_2 .

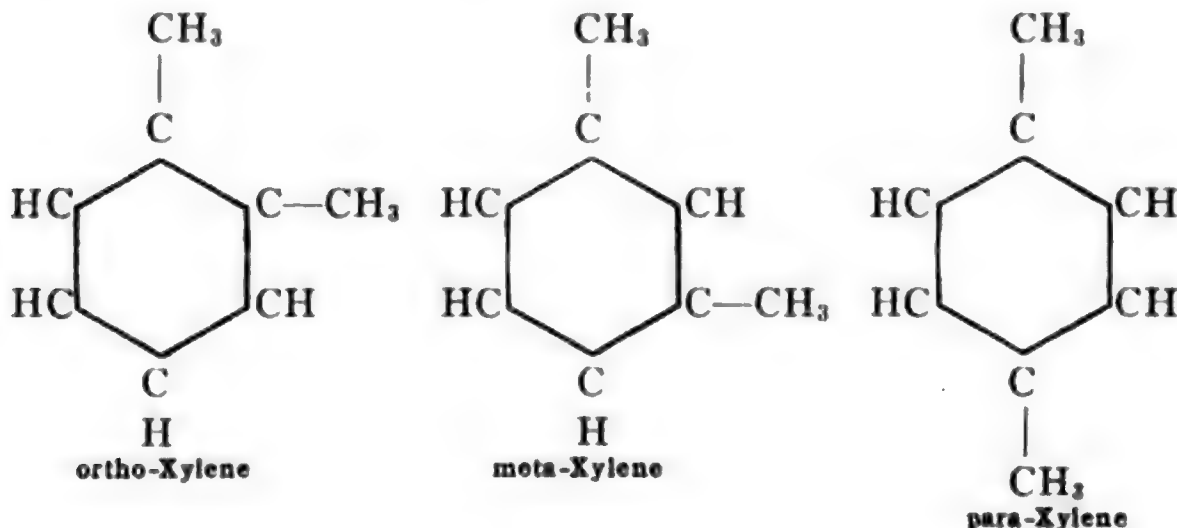


and



The three di-methyl benzenes are known as the **xylenes**, and the mono-ethyl benzene simply as **ethyl benzene**.

Orientation.—According to our theory the three known xylenes or di-methyl benzenes being di-substitution products must be represented by the three isomeric formulas due to the position of the substitution groups in the benzene ring as explained on p. 472. These are as follows:



As the three compounds are definite individuals possessing different properties such as melting point, boiling point, specific gravity, etc., the question now is, *to which of these compounds do we give one formula and to which another?* In other words, which one of the xylenes is the *ortho* compound, which is the *meta* and which the *para*? Without taking the matter up in its historical connection as to whether these names were first given to definite compounds, and the positions then determined; or whether they were first given to the definite positions and the compounds then named accordingly; we can simply state now, for the purpose of the following explanation, that the compound with the two substituting groups in the 1-2 *positions* is the *ortho* compound; the one with the 1-3 *positions* is the *meta* and the 1-4 is the *para*.

Ortho-meta- and para-Xylenes.—The three definite isomeric xylenes have the following physical properties which enable us to distinguish them from each other. For the present we may designate them simply as *A*, *B*, *C*.

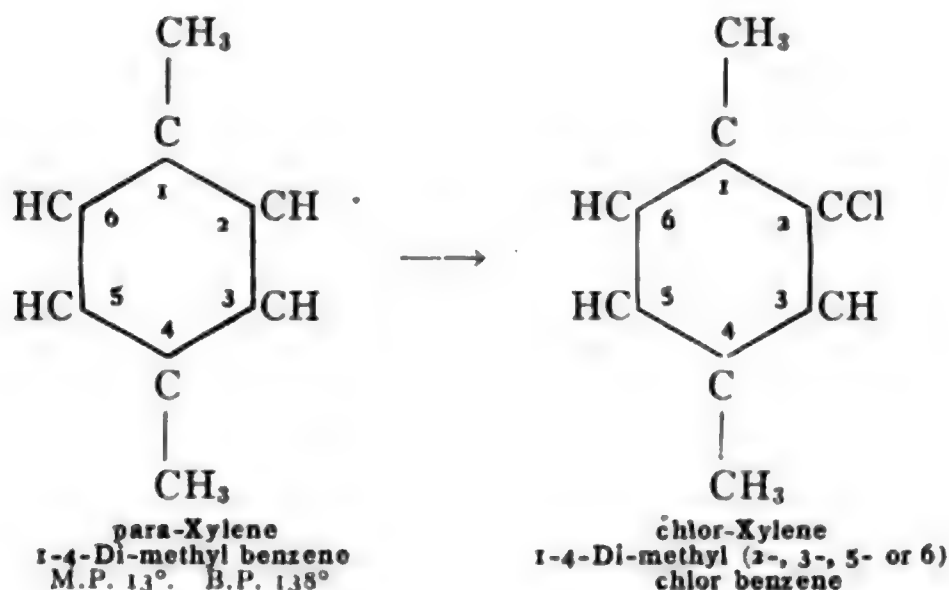
Xylene A has m.p. -28° ; b.p. 142° ; sp. gr. 0.893

Xylene B has m.p. -53° ; b.p. 139° ; sp. gr. 0.881

Xylene C has m.p. $+13^{\circ}$; b.p. 138° ; sp. gr. 0.880

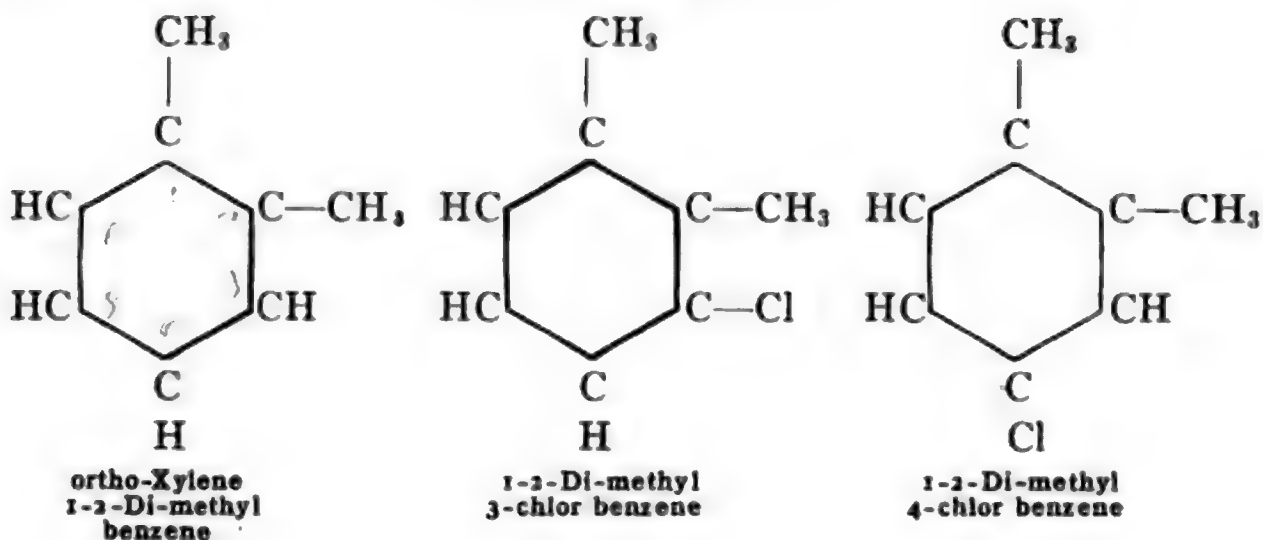
If we examine the formulas of the three isomers, we find that if in each one we substitute a third element or group in the benzene ring, each one of the original di-substitution products possess different possibilities as to the number of isomeric products that can be formed. Taking first the simplest case, we find for the **1-4 di-methyl benzene**, that all four of the remaining positions, viz., 2, 3, 5, 6, bear exactly the same relation to the already substituted methyl groups. It will make no difference then whether a *third* group is substituted in position 2, 3, 5 or 6. If the three xylenes are converted into mono-chlor-xylenes by substituting one chlorine atom into the benzene ring we may expect to find, that in one case, *only one product* is obtained no matter what method of preparation is used. This is the fact.

para-Xylene.—The xylene which boils at 138° and melts at 13° and the specific gravity of which is 0.880 yields only *one* chlor-xylene. The methyl groups must, therefore, be in the positions 1 and 4, and the chlorine may be either 2, 3, 5 or 6. This xylene must be then the *para* compound.



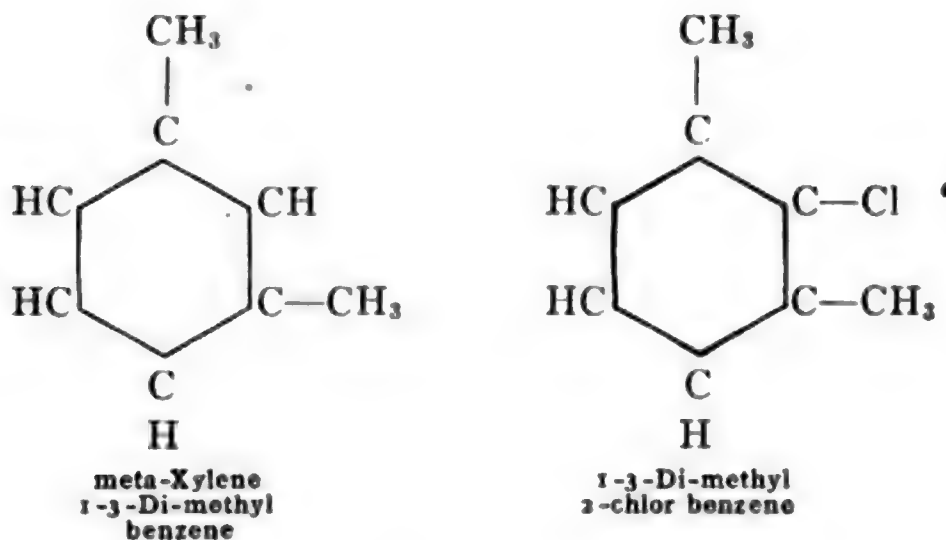
The other two xylenes yield not one only but more than one isomeric mono-chlor xylene. One of the xylenes yields *two* isomeric products while the other one yields *three*.

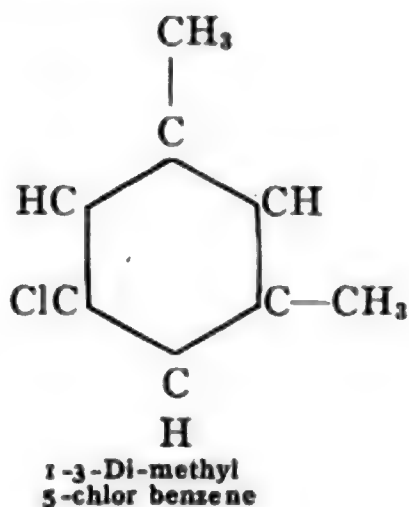
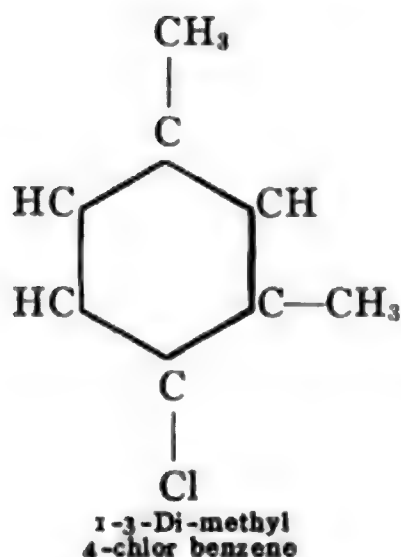
ortho-Xylene.—A similar examination of the formulas shows that with the **1-2-di-methyl benzene** *two* isomeric mono-chlorine substitution products are possible.



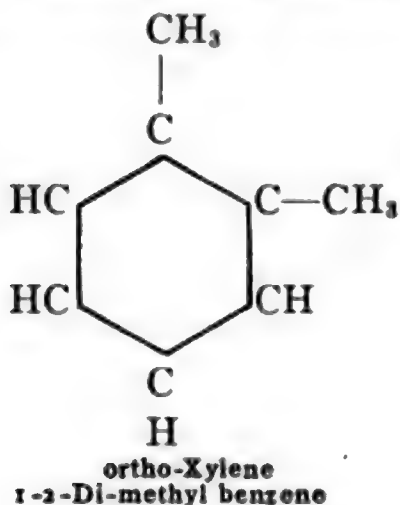
The position 6 is plainly in the same relation to 1 and 2 that 3 is, and 5 the same as 4 so that no other mono-chlor xylene is possible if the methyl groups are originally in positions 1 and 2. The xylene which boils at 142° and melts at -28° is the one which yields two and only two mono-chlor substitution products, and *it is, therefore, ortho-xylene.*

meta-Xylene.—The remaining isomeric xylene must of necessity be the meta compound, *i.e.* **1-3-di-methyl benzene**, but we have just as conclusive proof in this case as in the others. The xylene boiling at 139° and melting at -53° when converted into the mono-chlorine substitution product, with the chlorine in the ring, yields three isomeric compounds. From a study of the formulas it is readily seen, in this instance also, that the only di-methyl benzene which is possible of conversion into three isomeric mono-chlor xylenes is the *meta* or 1-3 compound.

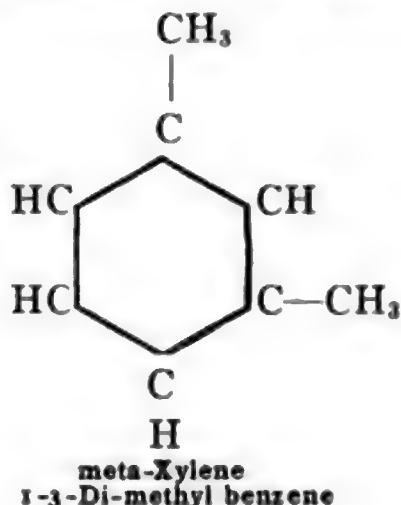




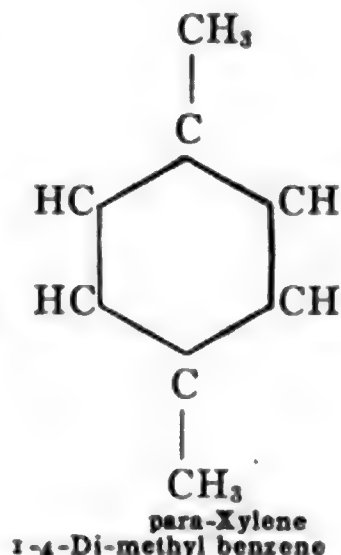
The position 6 is the same in relation to the two methyl groups as the position 4 so that no other isomer is possible. The xylene with the properties given is, therefore, **meta-xylene**. Writing the formulas for the three xylenes, with their properties, we have:



M.P. -28°
B.P. 142°
Sp. gr. 0.893



-53°
 139°
0.881

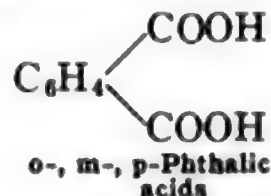
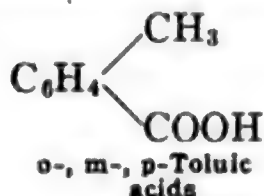
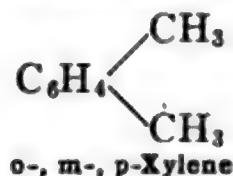


13°
 138°
0.880

Having thus determined in the case of the three di-methyl benzenes which is the *ortho*, which the *meta* and which the *para* compound, we have a shorter direct method for a similar proof in the case of any di-substitution product of benzene. It becomes necessary simply to convert the undetermined compound into xylene and whichever xylene is obtained we assume, unless there is proof of a migration of one of the groups, that in the original compound the two substituting groups occupied the same positions as the methyl groups in the resulting xylene. As the number of di-substitution products of benzene which have been

thus oriented has increased, the process becomes continually more simple, for it is only necessary to convert the unknown compound into any one of several known compounds. This method of determining which one of three isomeric di-substituted benzenes is the *ortho*, *meta* or *para* compound was first developed by **Körner**, who carried it out in connection with the **di-brom benzenes**. The process is known as **Körner's orientation**. A method was also developed by **Griess** with the di-amino benzoic acids. **Nölting** used the above method with the three xylenes as we have described it.

Oxidation of Xylene.—Just as toluene on oxidation has the *methyl* group converted into *carboxyl* yielding a *mono-carboxyl* or mono-basic acid, **benzoic acid**, so the xylenes by oxidation yield *di-carboxyl* or di-basic acids of the corresponding *ortho*, *meta* or *para* constitution. The two methyl groups are, moreover, possible of oxidation one at a time so that intermediate *mono-carboxyl* or *mono-basic* acids result in which one methyl group remains. The di-basic acids are known as **phthalic acids** and the mono-basic acids as **toluic acids**.



Hydrocarbons, C_9H_{12}

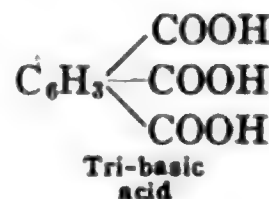
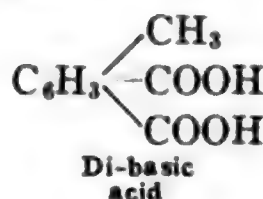
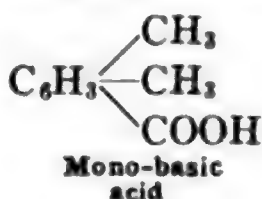
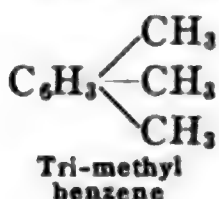
Vicinal, Unsymmetrical, Symmetrical, Tri-methyl Benzenes.—As was explained in discussing isomerism of the benzene substitution products (p. 473) **tri-methyl benzene** can exist in the three forms, *vicinal* or 1-2-3, *unsymmetrical* or 1-3-4, *symmetrical* or 1-3-5. All three of these are known and they are:

Mesitylene, 1-3-5-Tri-methyl benzene, *symmetrical*.

Pseudo-cumene, 1-2-4-Tri-methyl benzene, *unsymmetrical*.

Hemelithene, 1-2-3-Tri-methyl benzene, *vicinal*.

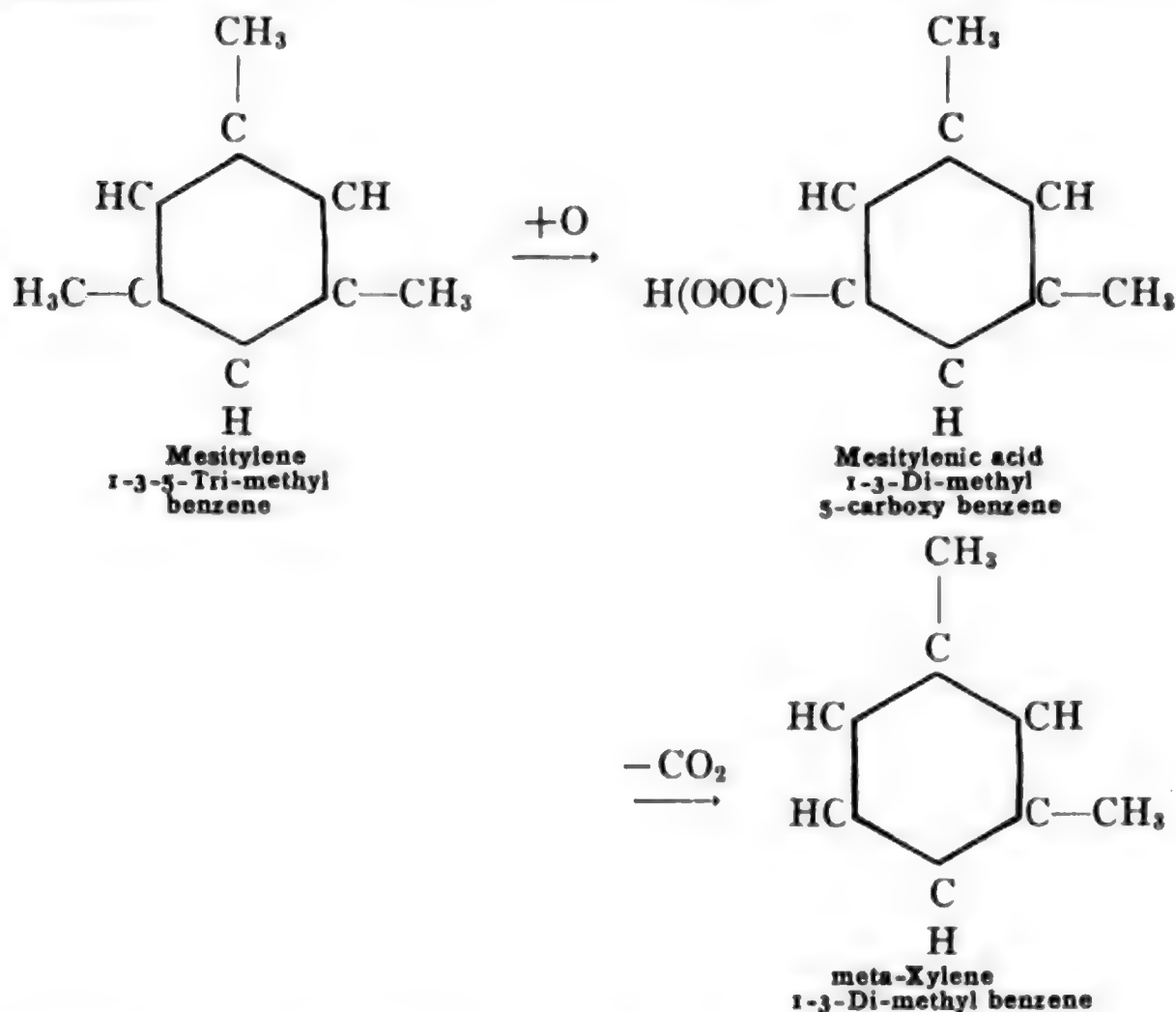
The proof that these three compounds are all tri-methyl benzenes is that by oxidation they each yield first a *mono-basic acid*, second a *di-basic acid* and finally a tri-basic acid.



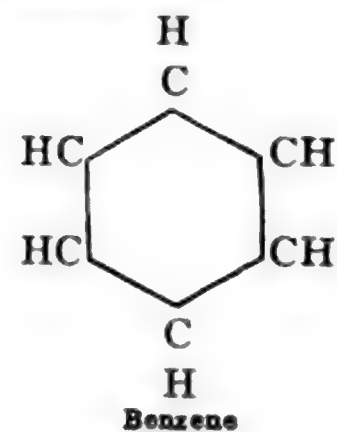
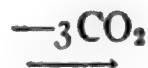
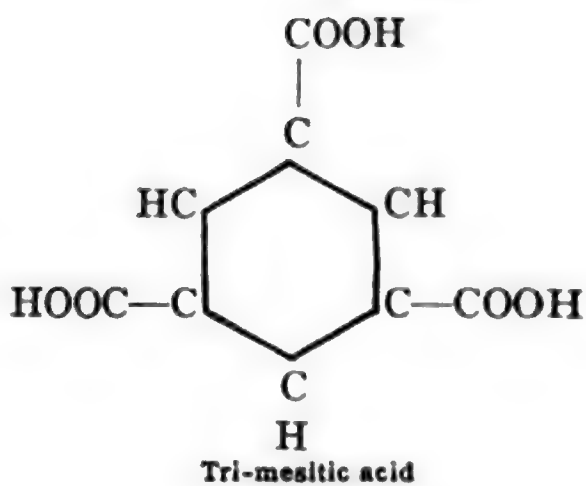
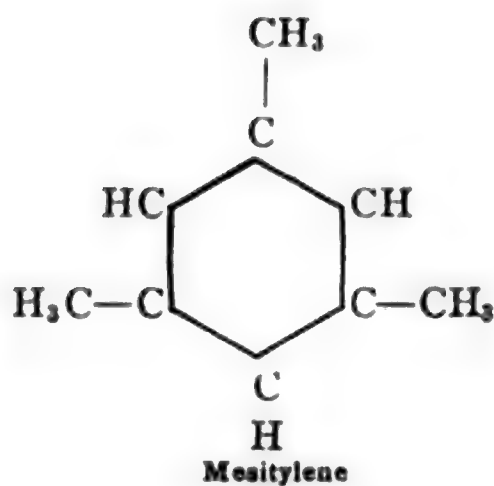
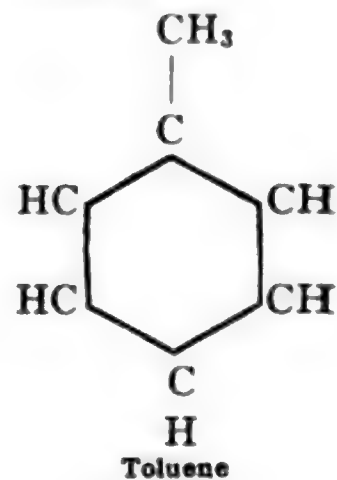
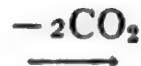
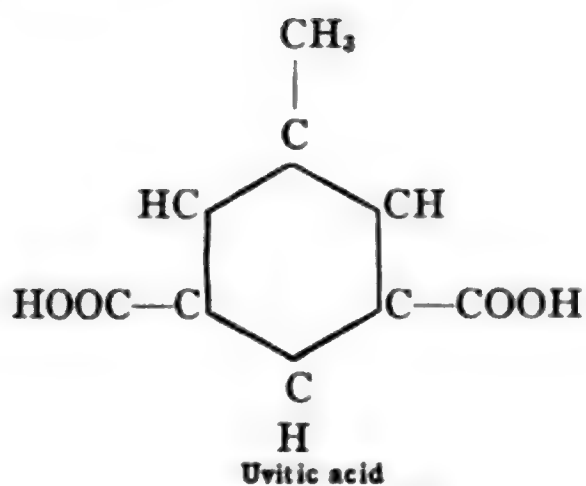
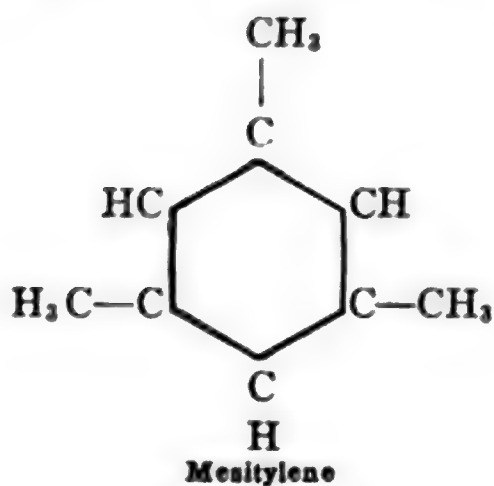
How can we prove, as in the case of the xylenes or di-methyl benzenes, which formula belongs to which compound?

Mesitylene, 1-3-5- Tri-methyl Benzene.—Taking up first mesitylene, two reactions show that this particular hydrocarbon must have the 1-3-5 or symmetrical constitution.

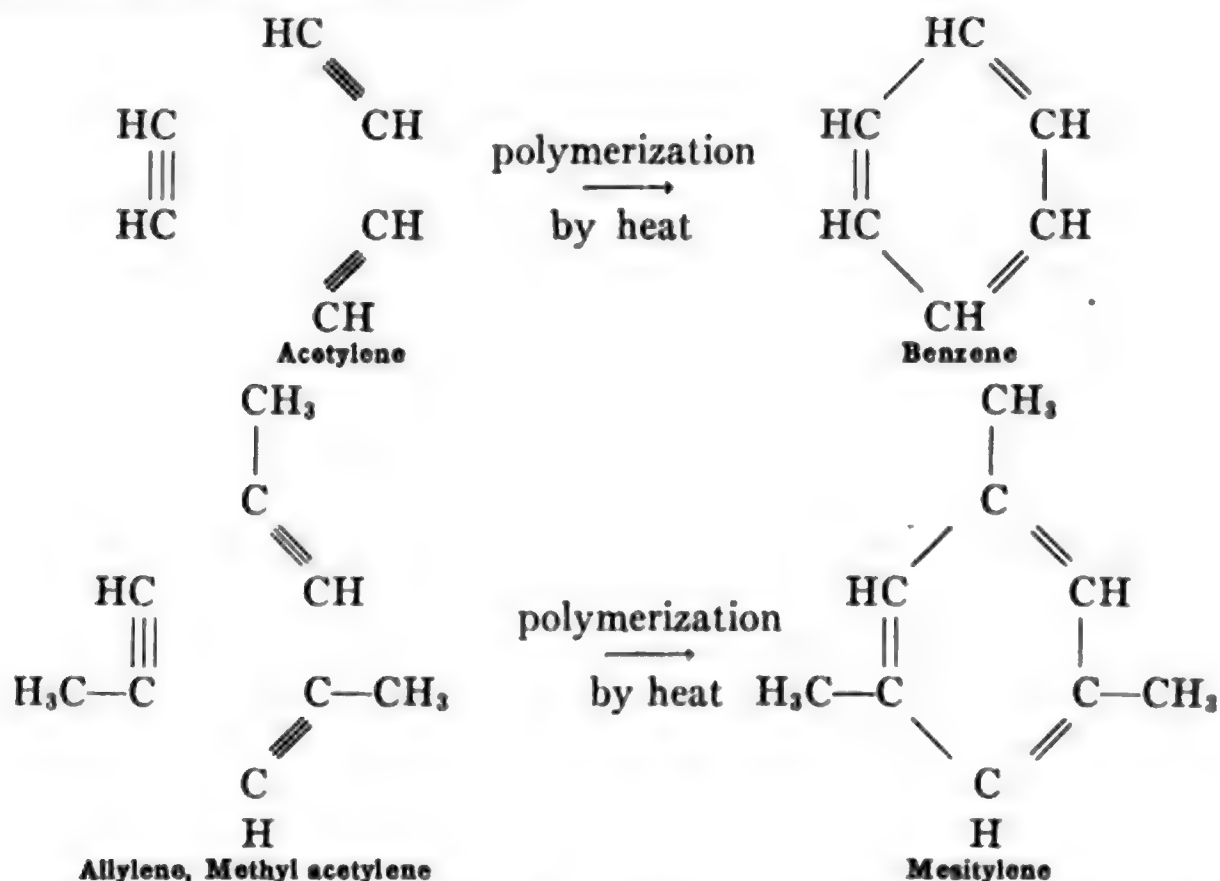
Oxidation of Mesitylene.—By oxidation it is converted into a mono-basic acid which on being heated with sodium hydroxide loses CO_2 and yields one of the di-methyl benzenes or xylenes. The particular xylene thus obtained is *always* meta-xylene or 1-3-di-methyl benzene.



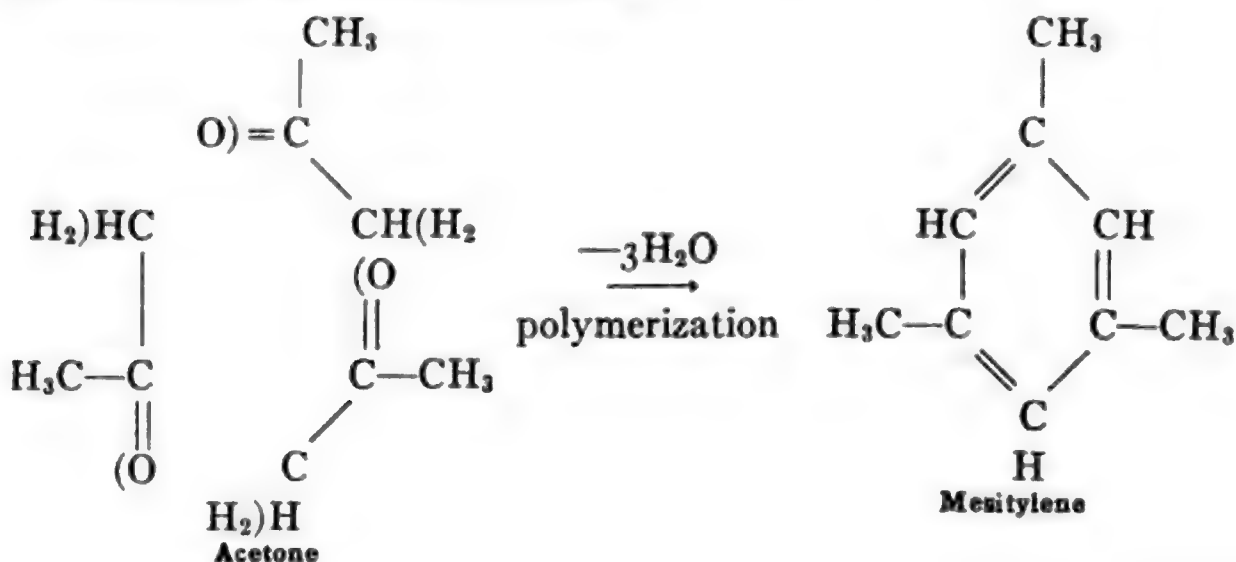
Clearly the only tri-methyl benzene that can thus *always* yield 1-3-di-methyl benzene is the one in which the three methyl groups are in the symmetrical positions, the 1-3-5 positions, so that whichever methyl group is oxidized the remaining two will be in the 1-3 positions. Further oxidation of mesitylene gives a di-basic acid which yields toluene, and complete oxidation of the methyl groups gives finally a tri-basic acid which yields benzene.



Synthesis of Mesitylene from Allylene.—The second proof of the symmetrical structure of mesitylene is its synthesis from **allylene** and also from **acetone**. The synthesis from allylene has already been spoken of in connection with the proofs of the structure of benzene (p. 478), and is exactly analogous to the synthesis of benzene by the polymerization of acetylene.



From Acetone.—By treating **acetone**, $\text{CH}_3-\text{CO}-\text{CH}_3$, with concentrated sulphuric acid, water is eliminated, polymerization takes place similar to that in the above reactions, and mesitylene is obtained. The reaction is represented as follows:

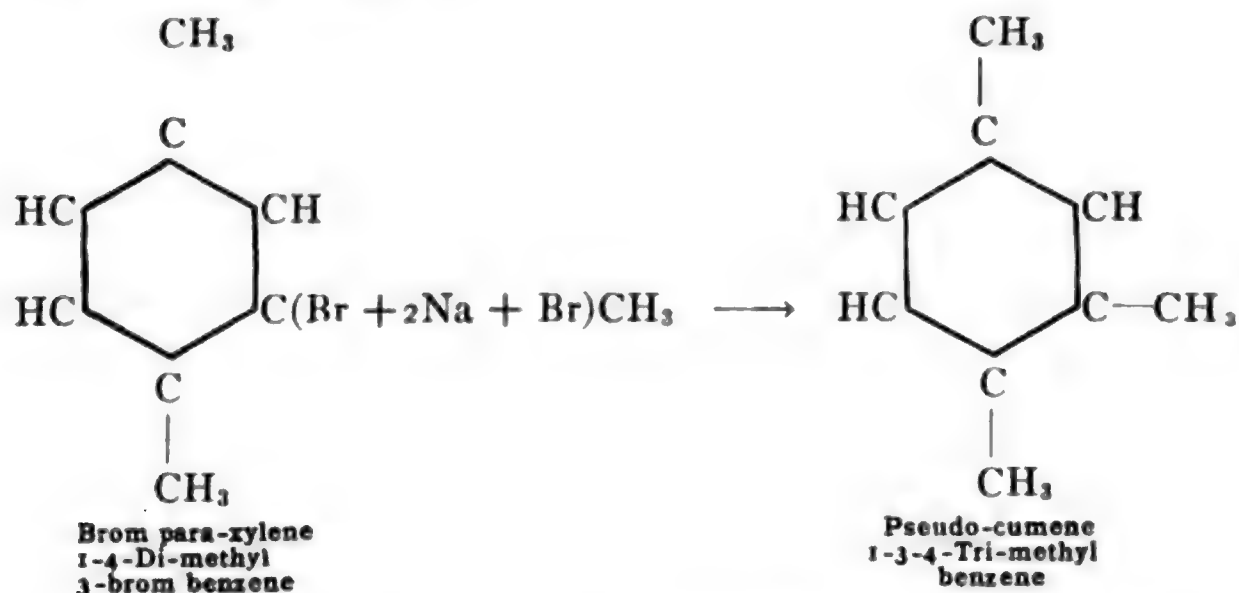


Substitution Products of Mesitylene.—A final proof of the structure of mesitylene is the fact that it yields only one mono-substitution product, and only one di-substitution product, when the substitution takes place in the benzene ring. This will appear clear on examination without writing out the formulas. As all three of the unsubstituted hydrogens of mesitylene remaining in the benzene ring are exactly alike in relation to the methyl groups it can make no difference which one or which two are substituted, the product will be the same. This condition exists only in the case of the 1-3-5-tri-methyl benzene and in neither of the other two, the 1-2-3, or the 1-3-4 compounds.

Mesitylene occurs in coal tar together with the other hydrocarbons we have considered. It is a liquid resembling benzene and toluene. Its boiling point is 165° .

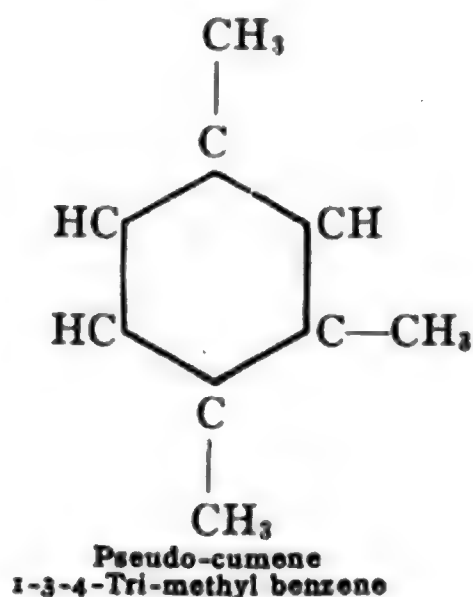
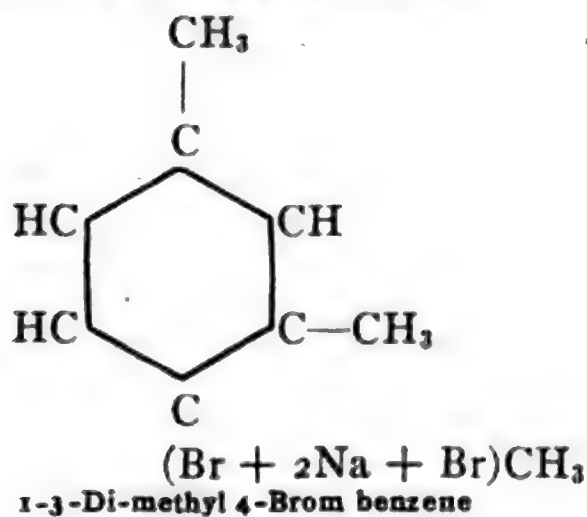
Pseudo-cumene, 1-2-4-Tri-methyl Benzene.—The second hydrocarbon, isomeric with mesitylene, and therefore tri-methyl benzene, is known as **pseudo-cumene**. It occurs also in coal tar, and resembles mesitylene in its properties. Its boiling point is 169° . Its structure is proven to be 1-2-4-tri-methyl benzene from the following reactions.

Pseudo-cumene from Brom para-Xylene and Brom meta-Xylene. **Brom para-xylene**, as will be recalled from the discussion of the constitution of para-xylene, exists only in one form as no isomeric compounds are possible. This substance, by means of **Fittig's synthesis**, yields pseudo-cumene, the constitution of which, therefore, can only be 1-3-4-tri-methyl benzene.



Brom meta-xylene exists in three isomeric forms (p. 473) and *one of*

these only, viz., the 1-3-di-methyl 4-brom benzene, yields pseudo-cumene by Fittig's synthesis.



Hemelithene, 1-2-3-Tri-methyl Benzene.—The third isomeric tri-methyl benzene is known as **hemelithene** and proves to be the 1-2-3 compound. It resembles the other two isomers, and like them is found in coal tar. It boils at 175° .

Propyl and Iso-propyl Benzenes.—In addition to the three tri-methyl benzenes we still have three isomeric hydrocarbons of the composition C_9H_{12} . These compounds are isomeric, depending on the substitution in benzene of other radicals than methyl. Substitution of one *propyl* radical for one benzene hydrogen atom gives us a compound of the same composition as that obtained by substituting three methyl radicals for three hydrogen atoms. As the propyl radical has two isomeric forms, viz., that of *normal propyl* and that of *isopropyl*, so we have the two substitution products, **propyl benzene**, $\text{C}_6\text{H}_5\text{—CH}_2\text{—CH}_2\text{—CH}_3$, and **iso-propyl benzene**, $\text{C}_6\text{H}_5\text{—CH}$ $\begin{matrix} \text{CH}_3 \\ \text{CH}_3 \end{matrix}$. The former

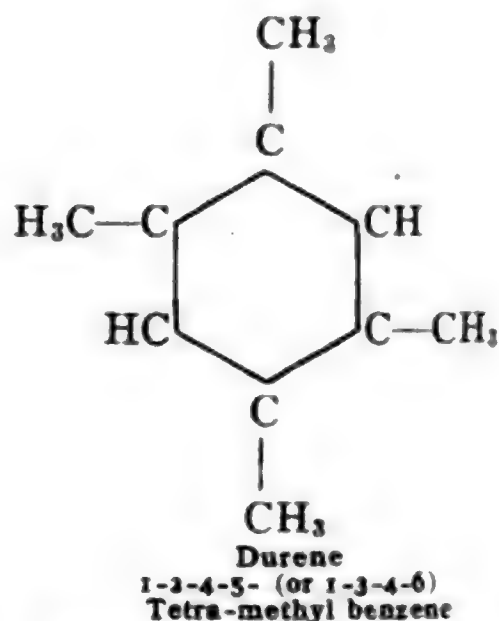
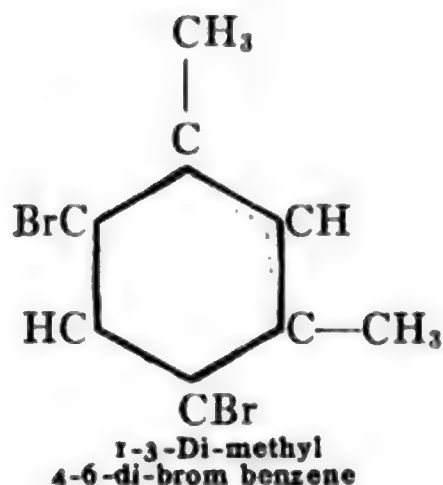
boils at 159° , and the latter at 153° . The **iso-propyl benzene** is also known as **cumene**. The third compound isomeric with the tri-methyl

benzenes is **methyl ethyl benzene**, C_6H_4 $\begin{matrix} \text{CH}_3 \\ \text{C}_2\text{H}_5 \end{matrix}$, which exists in three forms, *o*, *m*, and *p*.

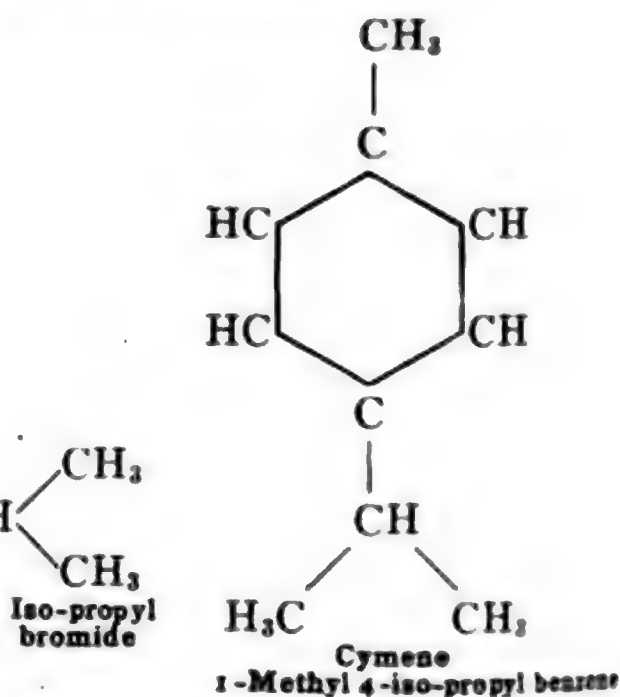
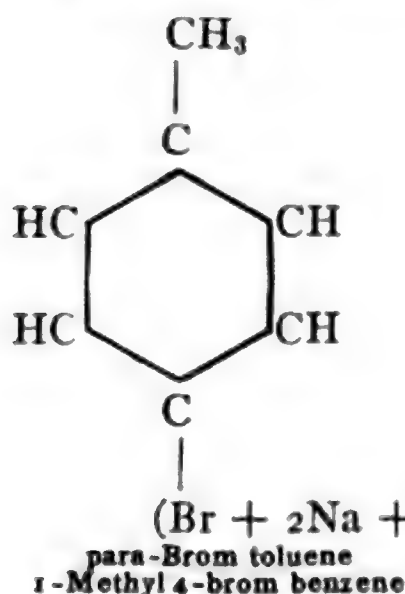
Hydrocarbons, $\text{C}_{10}\text{H}_{14}$

Durene and Cymene.—Two hydrocarbons of this composition are of importance because of their close relation to **turpentine** and **camphor**.

Durene is the **1-2-4-5-tetra-methyl benzene**. It has a camphor-like odor and is found in coal tar. It can be made from one of the di-brom meta-xylenes, viz., the **1-3-di-methyl 4-6-di-brom benzene** by **Fit-tig's synthesis**.



Cymene. 1-Methyl 4-Iso-propyl Benzene.—Cymene, the only other isomeric hydrocarbon of the composition $C_{10}H_{14}$, which we shall consider, is shown to be 1-methyl 4-iso-propyl benzene, by its synthe-sis from **para-brom toluene** and **isopropyl bromide**.



Cymene is found in thyme oil, eucalyptus oil, and Roman cummin oil. It is also obtained by heating camphor with phosphorus pentoxide and from turpentine by reduction with iodine.

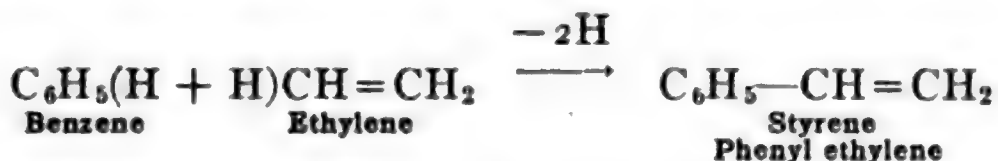


These relationships will be discussed more fully when we consider turpentine and camphor, and it will be found that these two important substances have the same ring structure as cymene. The other hydrocarbons of the benzene series need not be discussed in detail. It is sufficient to know of their existence in the homologous series as given in Table (p. 476).

Hydrocarbons, C_nH_{2n-8} and C_nH_{2n-10}

It is best to speak at this time of hydrocarbons derived from benzene by the substitution in the ring of *unsaturated* open chain radicals. Just as the homologues of benzene are prepared by substitution of a saturated paraffin radical, methyl, ethyl, propyl, etc., in the benzene ring, so other series of hydrocarbons have been obtained by substituting radicals of the unsaturated open chain hydrocarbons of the ethylene and acetylene series. These new compounds will be poorer in hydrogen than the benzene series by two and four atoms respectively.

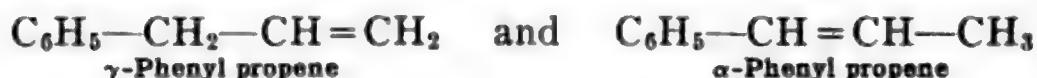
Styrene, Phenyl Ethylene.—The first of these hydrocarbons is known as **styrene**. It is obtained from *storax*, a resin found in the plant, *Styrax officinalis*. It is also present in coal tar. It is related to, and also prepared from, **cinnamic acid**, an important acid to be considered later. Styrene is a liquid boiling at 140° . Its constitution is proven by its synthesis from benzene and ethylene when a mixture of the two compounds is passed through a red hot tube.



The radical (C_6H_5-), is known as *phenyl* and styrene is, therefore, **phenyl ethylene**, naming it as a substitution product of ethylene. As a benzene substitution product its name is **ethylenyl benzene**.

Phenyl Propene or Propenyl Benzene.—While the next higher member, which is phenyl propene, $C_6H_5-CH_2-CH=CH_2$, is not important in itself we shall find later (p. 623) that derivatives of it are present in some very valuable *essential oils* found in plants. A case of isomerism is present here which it is well to mention. Two compounds are known both of which correspond to phenyl propene, the isomerism being due to the position of the double bond, or if we look at the compound as a phenyl substitution product of propene, it is due to the posi-

tion in which the phenyl group is substituted in propene. The two formulas are as follows:



This is exactly analogous to the isomerism of the halogen propenes (p. 164).

Phenyl Acetylene.—The only other hydrocarbons of this kind that we shall mention are **phenyl acetylene**, $\text{C}_6\text{H}_5\text{—C}\equiv\text{CH}$, which is a liquid boiling at 140° , and **α -phenyl propine**, $\text{C}_6\text{H}_5\text{C}\equiv\text{C—CH}_3$.

These hydrocarbons naturally possess the properties of both benzene and unsaturated open chain compounds.

COAL TAR

“Coal tar; at first a troublesome waste product, now, its derivatives, the host of aromatic compounds, are applicable in numberless and daily increasing ways in the sciences, arts and industries. They are indispensable as aids in the hands of the chemist, the physiologist, the bacteriologist and the doctor, and are serviceable in the multiform needs of the dyeing industry, painting, photography and the manufacture of explosives. They are the artificial dyes, the synthetic medicines, the aroma of plants and of the musk ox, food stuffs hundreds of times sweeter than sugar, and destructive explosives.”

Thus speaks **Heinrich Caro**,¹ one of the prominent workers in the development of the coal tar industry in Germany.

All of the hydrocarbons which we have mentioned, with the exception of phenyl acetylene, are found in coal tar. In addition, other hydrocarbons which we shall consider later, and several derivatives, especially hydroxyl and amino derivatives, are likewise obtained from it. It is, therefore, of great importance as a source of benzene compounds, and a consideration of the subject from a commercial standpoint is best made now.

Illuminating Gas.—A large part of the illuminating gas used in our cities is made by distilling soft or bituminous coal.

Distillation of Coal.—In this process of manufacture the coal is heated in large iron or brick stills out of contact with the air. By such a distillation the coal is broken down into three main groups of substances, gases, liquids and solids.

Gaseous Products.—The gaseous product is composed largely of **hydrogen, methane, carbon monoxide, carbon dioxide, nitrogen,**

¹ Ber. 25 (c), 955; 1892.

ammonia and **hydrogen sulphide**, with small amounts of hydrocarbons other than methane including **acetylene** and **benzene**.

Liquid and Solid Products. Coal Tar.—The liquid products consist of **water** holding **ammonia** in solution and a heavy oil-like substance known as **coal tar**. The solid residue left in the retort is known as **coke**, and contains the unburned and uncombined carbon together with the non-volatile constituents of the coal representing the mineral matter or ash.

Coal $\xrightarrow{+ \text{heat}}$	gas	Methane, CH_4
		Hydrogen, H_2
		Carbon monoxide, CO
		Carbon dioxide, CO_2
		Nitrogen, N_2
		Ammonia, NH_3
		Cyanogen, $(\text{CN})_2$
		Hydrogen sulphide, H_2S
	Other hydrocarbons, C_2H_2 , C_6H_6 , C_{10}H_8 , etc.	
	liquid	Ammoniacal liquor (water + NH_3 , etc.)
		<i>Coal Tar</i>
solid	Coke	

Composition of Illuminating Gas.—The volatile liquid and gaseous products are first led through cool tubes or condensers where the liquid portion is retained. The gaseous product is then washed with water, and purified to remove cyanogen, ammonia, hydrogen sulphide and most of the carbon dioxide. The washed gas, containing methane, hydrogen, carbon monoxide, some of the carbon dioxide, nitrogen and the miscellaneous hydrocarbons in small amount, is the illuminating gas as used.

Purified illuminating gas. Approximate composition.	{	Methane, CH_4	36 per cent
		Hydrogen, H_2	47 per cent
		Carbon monoxide, CO	8 per cent
		Nitrogen, N_2	4 per cent
		Carbon dioxide, CO_2	1 per cent
		Acetylene, C_2H_2	4 per cent
		Benzene, C_6H_6	
		Naphthalene, C_{10}H_8	

Ammonia.—The liquid portion, held by the condenser, consists of the **ammoniacal liquor** (water solution of ammonia and some other compounds) and **coal tar**, and is easily separated into the two constituents. The ammoniacal liquor together with the wash water from the purification of the gas is known as gas liquor and forms the large commercial source of **ammonia** and **ammonium salts**.

Gas Liquor Salt, Ammonium Sulphate.—When this liquor is neutralized with sulphuric acid, or if the wash water contains sulphuric acid, it yields on evaporation a crystalline mass known as *gas liquor salt*. This salt is largely **ammonium sulphate**, and is the crude ammonium sulphate used in the fertilizer industry as the chief source of ammonia nitrogen. The coal tar after separation from the ammoniacal liquor is subjected to fractional distillation.

Coke.—The solid non-volatile residue or coke is used as fuel, especially in the iron and steel industry. Most of the coke so used is made in *coke ovens* in which the gas and liquid products were originally allowed to escape into the air and were wasted. In recent years much of the coal tar formerly wasted is now recovered. Thus with the development of our knowledge of the benzene series of compounds, which include valuable dyes, explosives, medicines, etc., this substance that was formerly thrown away has become a most important industrial product. So important are the compounds obtained, either directly or indirectly, from it that the name coal tar has become an adjective of common use and significance as shown by the terms, *coal tar industry*, *coal tar products*, *coal tar dyes*.

Chemically coal tar is a highly complex mixture of many compounds, but fortunately these may be separated and obtained in a pure condition by fractional distillation and treatment with acids and alkalis. The detailed study of most of these compounds will be taken up later, but before discussing their separation from coal tar it will be well to describe their general character. They belong to three classes, viz. (1) neutral compounds or *hydrocarbons*, (2) acid compounds or *phenols*, and (3) basic *nitrogen compounds*. The hydrocarbons obtained from coal tar are the ones we have already studied, viz., **benzene**, **toluene**, **xylene** and **mesitylene**, and, in addition to these, **naphthalene**, **anthracene** and **phenanthrene** which are related to benzene but belong to other more complex series. The acid compounds are known by the general name of *phenols* from the simplest member **phenol** or **carbolic**

acid. They are hydroxyl substitution products of the hydrocarbons. The ones obtained from coal tar are **phenol**, **cresols** or **hydroxy toluenes**, **xlenols** or **hydroxy xylenes** and **naphthols** or **hydroxy naphthalenes**. The basic compounds are amino substitution products of the hydrocarbons, viz., **aniline** or **amino benzene**, of which there is only a very small amount present, and heterocyclic nitrogen bases known as **pyridine** and **quinoline**. The five most important compounds are **benzene**, **toluene**, **naphthalene**, **anthracene** and **phenol** which together are obtained in a yield of 10 to 15 per cent of the coal tar. The remaining 85 to 90 per cent of the tar constitutes the residue left after it is distilled. This residue is known as *pitch* or *tar* and is used to manufacture some heavy oils used as crude creosote for impregnating wood paper, etc., and as tar for road-making, etc.

Fractional Distillation of Coal Tar.—The distillation of the coal tar is carried out in iron retorts, and fractions distilling at certain temperatures are obtained. These fractions vary somewhat in different works and with different tars, but the following may be given as a general result.

FRACTIONAL DISTILLATION OF COAL TAR

Product	Distillation temperature
I. Light oil (crude naphtha)..... (Principally benzene hydrocarbons with some phenols, some bases and some naphthalene)	Below 170° or 210°
II. Middle oil (phenol or creosote oil)..... (Principally phenols, 25 per cent, and naphthalene, 50 per cent)	170° or 210° to 230° or 240°
III. Heavy oil..... (Principally naphthalene and anthracene)	230° or 240° to 270°
IV. Anthracene oil..... (Most of the anthracene)	Above 270°
V. Pitch or tar.....	Residue

Fraction I, known as *light oil* because it floats on water (sp. gr. = 0.975), contains some ammoniacal liquor from which it separates. The separated oil contains mostly hydrocarbons of the benzene homologous series, but there are also present in it some phenols, some basic compounds and some naphthalene. The acid and basic compounds may

be removed at this stage or after the next fractionation by treatment with alkali and then with acid. The alkali forms soluble salts with the phenols which may then be removed by washing with water; and similarly the basic nitrogen compounds are removed by means of acid and then washing with water. The treated and washed light oil is then subjected to a new fractional distillation. The fractions usually collected are:

FRACTIONAL DISTILLATION OF LIGHT OIL

Product	Distillation temperature
A. 90 Per cent benzene..... (Benzene with some toluene)	80° to 110°
B. 50 Per cent benzene..... (Toluene and xylene with some benzene)	110° to 140°
C. (Xylene and mesitylene)	140° to 170°
D. Phenol oil..... (Phenols)	170° to 195°
E. (Sometimes combined with D)..... (Naphthalene)	Residue

90 Per Cent Benzene.—Fraction *A* contains actually about 70 per cent of **benzene** and about 30 per cent of **toluene**. Commercially it is known as *90 per cent benzene* because 90 per cent of it distils below 100°.

50 Per Cent Benzene.—Fraction *B* contains about 46 per cent of **benzene**, the rest being **toluene** and some **xylene**. Commercially it is termed *50 per cent benzene* because 50 per cent of it distils below 100°. Fraction *C* contains the higher hydrocarbons **xylene** and **mesitylene**, etc., and practically no benzene or toluene. If treatment with alkali and acid has not been previously carried out these fractions are now subjected to such treatment to remove phenols and basic compounds and are then again fractionated to obtain the pure hydrocarbons. Most of the **phenols** are present in fraction *D*. This fraction is often not collected separately, but becomes part of the residue which is combined with the middle oil. The *middle oil* contains often as much as 50 per cent of **naphthalene**, which crystallizes out if the oil is cooled, and is separated by means of a centrifuge. The oil thrown off from the centrifuge yields a little benzene, toluene and

xylene in a first fraction which is mixed with fresh light oil and fractionated with it. The second fraction from the middle oil contains mostly **phenols** with some bases which are separated in the usual way. The third fraction will contain some naphthalene not obtained in the first crystallization. The residue from the middle oil contains some **anthracene** and is combined with the heavy oil. The **heavy oil** which contains principally **naphthalene**, about 28 per cent, and **anthracene** but also some **phenols**, about 16 per cent, is separated into three fractions by distillation in a vacuum. The first contains the **phenols**, the second the **naphthalene** and the residue contains principally **anthracene** which is separated by means of hydraulic pressure. The final coal tar fraction or *anthracene oil* contains **anthracene** and some **phenanthrene**. The latter is extracted by means of petroleum ether as a solvent, and from the residue the anthracene is separated by pressure.

In the preceding discussion of the recovery and fractional distillation of coal tar, in the process of coal gas manufacture, we have considered only the direct cooling method. While this is the method commonly used heretofore, the more progressive concerns are utilizing the principle of fractional cooling and washing such as has been devised by **Feld**. The general process may be briefly described as follows: Instead of being cooled in one condenser to the ordinary temperature of water, 15° to 20°, thus condensing all of the liquid products into one tar, the vapors given off by distilling the coal are fractionally cooled and washed. The first cooling is only to about 160° to 200°. This yields a coal tar as in the other method but the amount is necessarily small. After cooling to this temperature the rest of the cooling is carried out in a series of condensers each one a little lower in temperature than the preceding. These condensers also contain a washing liquid through which the gas passes and to which the gas gives up certain of its constituents. In the higher temperature condensers the wash liquid is successively heavy oil, middle oil and light oil. The temperature of these condensers or washers is about as follows: 160°, 80°, 60°, and 40°. In them most of the coal tar products are retained and are later separated by fractionating the wash liquids with the similar oils obtained from the coal tar. In the next condensers, the temperatures of which run about as follows: 38°, 34°, 18°, the wash liquid is water. These water wash liquors absorb from the gas practically all of the ammonia, hydrogen

sulphide, and cyanogen gases and also separate out from the gas some of the benzene and naphthalene which are still in solution in the gas. As a result of this fractional cooling and washing a part of the coal tar is at once fractionated and the coal gas issues from the final washer practically pure and nearly free from tar constituents. The total yield of tar products is increased over that obtained by the direct cooling process and the amount of benzene and naphthalene left in the illuminating gas is diminished as much as is practicable for a gas of proper illuminating power. For details of this process, which it is not advisable to consider here, the student is referred to technical works such as **Wagner**, "Coal Gas Residuals."

Yield from Coal Tar.—The yield of coal tar in the original distillation of the coal is about 2 to 5 per cent, but it depends upon many physical or mechanical factors such as temperature and pressure of the distillation, the form of the still, the length of time and the temperature to which the volatile products are heated, etc. Approximate yields from the redistillations of the coal tar may be stated as follows:

Coal tar, 100 per cent	Benzene, toluene and xylene.....	1.0 - 2.5 per cent
	Naphthalene.....	4.0 - 10.0 per cent
	Anthracene.....	0.25 - 2.0 per cent
	Phenol.....	0.4 - 0.5 per cent
	Cresols.....	2.0 - 3.0 per cent
	Pyridine and quinoline.....	0.2 - 0.3 per cent
	Creosote oil.....	25.0 - 30.0 per cent
	Pitch or tar.....	50.0 - 60.0 per cent

Coal Tar Industry.—The importance of the coal tar industry may be gathered from consideration of a few statistics. Germany produced, in 1890, 100,000 tons of coal tar from gas works and 60,000 tons from coke ovens. England produced 700,000 tons of coal tar from all sources. Thus England leads in the production of coal tar. Germany, however, leads all other countries in the utilization of coal tar, importing a large part of that produced elsewhere. In 1890 Germany had twenty-one factories thus utilizing coal tar and the value of the products made from it amounted to \$25,000,000. Since 1914 the production of coal tar and its utilization in the United States have increased tremendously. This development has been so rapid that accurate figures are impossible to obtain.

Theories of Formation of Benzene, etc.—Theories of the formation of these benzene products in the distillation of coal have been investigated principally by Berthelot, and his conclusions are, in general: In the first place, coal decomposes by heat yielding simple paraffin compounds such as methane, ethylene, acetylene, alcohol, acetic acid, etc. These compounds when subjected to higher temperatures polymerize into benzene, and the higher hydrocarbons naphthalene, anthracene, phenanthrene, etc., and into derivatives of these such as phenol, aniline, pyridine, etc.

B. DERIVATIVES OF BENZENE HYDROCARBONS

I. HALOGEN DERIVATIVES

The derivatives of the benzene series of hydrocarbons may be grouped in very nearly the same classes as the derivatives of the aliphatic hydrocarbons, as follows:

A. Halogen.....	derivatives
B. Sulphuric and sulphurous acid.....	derivatives
C. Nitric and nitrous acid.....	derivatives
D. Ammonia.....	derivatives
E. Azo and other intermediate nitrogen.....	derivatives
F. Di-azo.....	derivatives
G. Ring hydroxyl.....	derivatives (Phenols)
H. Side chain hydroxyl.....	derivatives (Alcohols)
I. Aldehydes and ketones.....	
J. Acids.....	
K. Substituted acids.....	

In considering these different classes it will be found that they bear the same relationship to the hydrocarbons from which they are formed as do the corresponding derivatives of the aliphatic series to their respective hydrocarbons.

While the general methods of preparation and the characteristic reactions of analogous classes in the two series of derivatives are sometimes the same they are more often distinctly different. The *halogen derivatives* of the benzene series are not formed from the hydroxyl derivatives, as in the aliphatic series, but by direct action of the halogen. Their reactions also are different. The *sulphuric acid* and *nitric acid* derivatives which, in the aliphatic series, are formed with difficulty, and are not generally important; in the benzene series are formed with ease and are extremely important and very reactive. The *ammonia derivatives* which, in the aliphatic series, are formed from the halogen compounds; in the benzene series are formed by reducing the nitric acid derivatives. The *azo* and *di-azo* derivatives of the benzene series are among the most important compounds we shall

study; whereas in the aliphatic series only a few compounds of the class are known. The *hydroxyl derivatives* of the benzene series are of two distinct classes; one of which includes true *alcohols* analogous to those of the aliphatic series, the other includes compounds known as *phenols*, which are acid compounds. The *aldehydes* and *ketones* of the two series are in general formed by similar reactions and are of similar character though in the benzene series a new class, known as *quinones*, are entirely distinctive. The *acids* of the benzene series while they may be prepared by the oxidation of aldehydes as in the aliphatic series are often prepared by the oxidation of a methyl group to carboxyl.

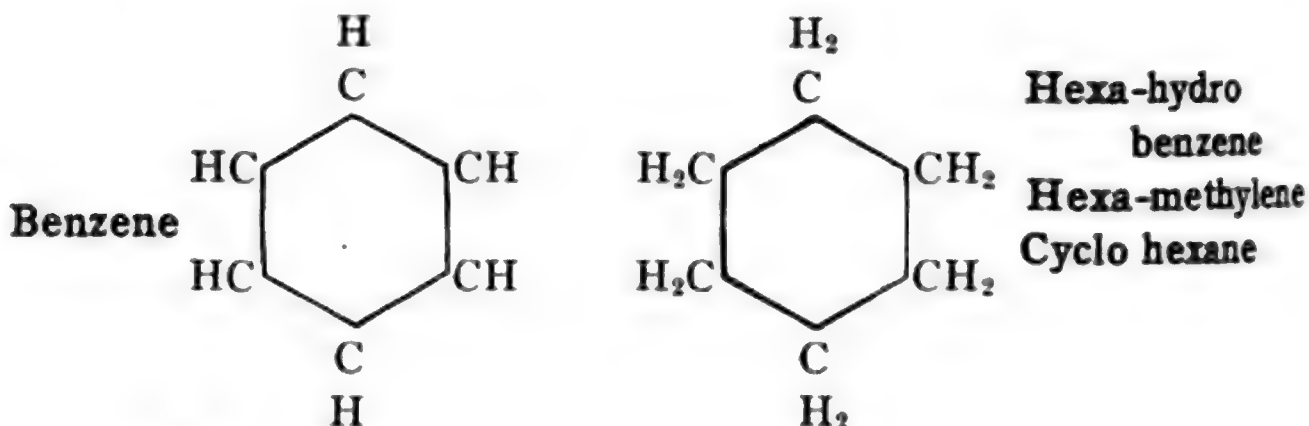
On the other hand, the ammoniacal character of the ammonia derivatives, the alcoholic character of the true benzene alcohols and the general reactions of aldehydes and acids are alike in the two series of derivatives. What has just been said applies in most cases to those derivatives of the benzene series in which the compound is formed by substitution in the benzene *ring*. As we shall find later the derivatives of this series are of two kinds: (*a*) those in which substitution is in the ring, and (*b*) those in which substitution is in the side chain of the benzene homologues. These latter compounds are wholly analogous to corresponding aliphatic compounds as in the case of the true alcohols of the benzene series just mentioned. The order of taking up the different classes varies in the two series because of the ease of preparation and the importance of the sulphuric and nitric acid derivatives of the benzene series.

HALOGEN BENZENES

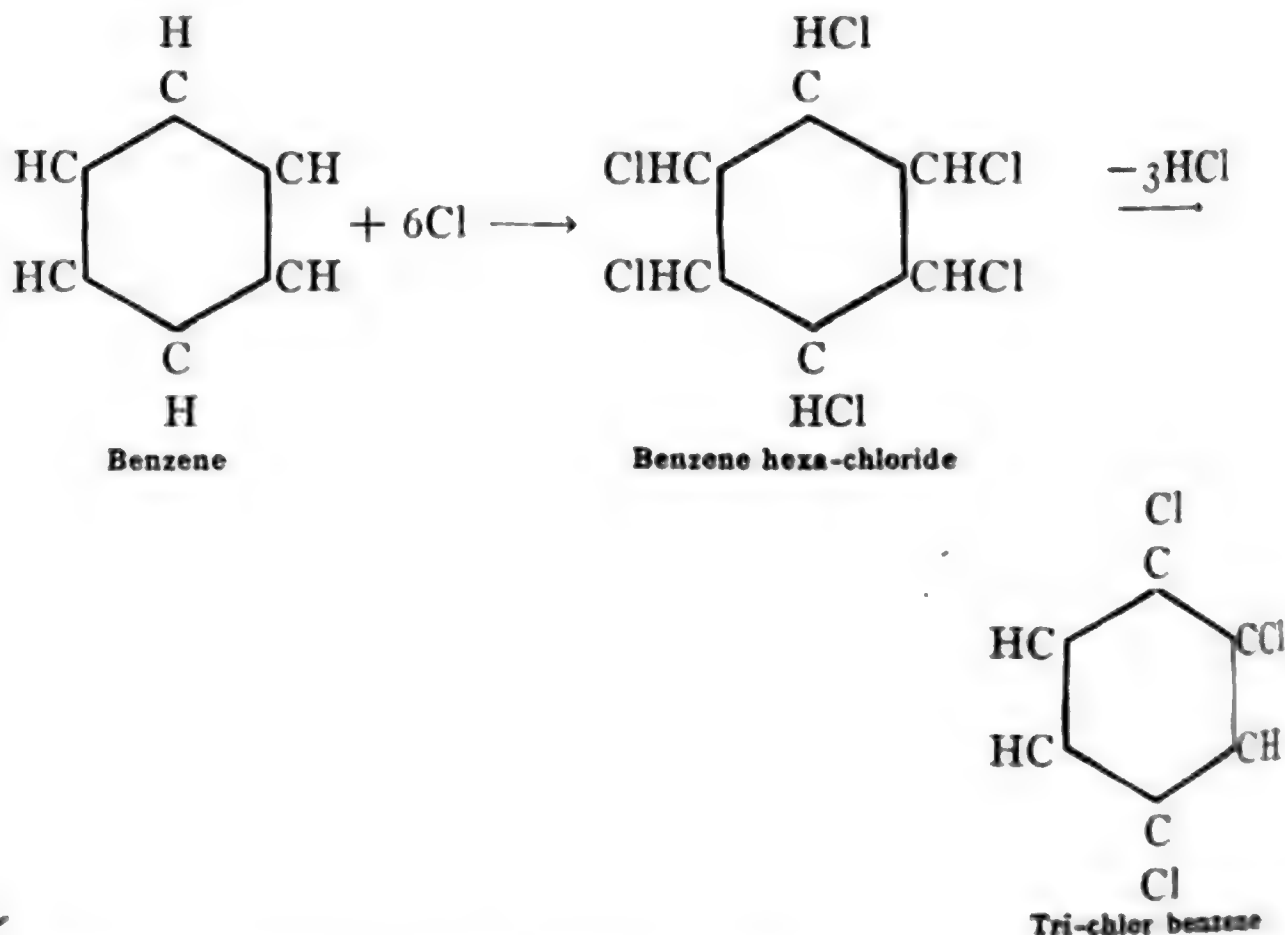
We speak of the halogen *derivatives* because in the benzene series we have both addition products and substitution products. While benzene, as we stated previously, does not act like an unsaturated compound it does, nevertheless, form relatively unstable addition products though with more difficulty than substitution products. The addition products of the unsaturated hydrocarbons of the paraffin series are very easily formed and are stable compounds; in fact are identical with substitution products of the saturated series.



Hexa-hydro Benzene.—With hydrogen benzene forms a hexa-hydro addition product which is **hexa-methylene** or **cyclo-hexane**.

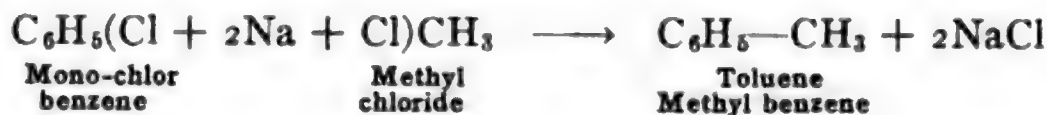


Benzene Hexa-chloride.—When chlorine acts upon benzene in the sunlight **benzene hexa-chloride** is formed which is unstable readily losing 3HCl, yielding **tri-chlor benzene**, a stable tri-chlor substitution product.



Halogen Substitution Products.—When, however, chlorine acts on benzene in diffused light, substitution products are formed directly. This takes place more readily in the presence of halogen carriers, e.g. **ferric chloride, FeCl_3 ; aluminium bromide, AlBr_3 ; antimony chloride,**

Fittig's Reaction.—The most important reaction of the benzene halogen substitution products is what is known as **Fittig's reaction**, by means of which a paraffin chain may be substituted in the benzene ring, and benzene homologues prepared.



This is exactly analogous to the preparation of paraffin homologues by the Wurtz reaction.



Benzene from Mono-halogen Benzene.—Nascent hydrogen removes the halogen and reforms benzene.



A very interesting fact is observed in connection with the formation of the *di-halogen substitution products*. When **di-brom benzene** is prepared it is *almost entirely* the *para* compound which is formed, but at the same time a *little* of the *ortho* but *none* of the *meta* compound is obtained. While it cannot be stated as a definite law still it may be given as a general empirical rule that when the first substituting group in a benzene ring is *Cl, Br, I, OH, CH₃*, or any aliphatic radical, the second group entering the ring will take either the *para* or the *ortho* position. Usually both compounds result, with a larger amount of the *para* product in most cases, but *no meta* compound. On the other hand, if the first substituting group is one of the following, viz., *CHO, COOH, CN, NO₂, SO₂OH*, then a second group entering the ring takes the *meta* position only. Why this is so is not definitely known though stereo chemistry offers an explanation.

With the exception of the iodine substitution products of benzene, which deserve special consideration, the halogen products will be mentioned only in a tabular statement of their properties. They are not of any particular importance or interest.

TABLE XVIII.—HALOGEN SUBSTITUTION PRODUCTS OF BENZENE

		M.P.	B.P.
Mono-chlor benzene, C_6H_5Cl	Liquid	— 44.9°C.	132°C.
Penta-chlor benzene, C_6HCl_5	Solid	85.0°C.	275°C.
	colorless needles		
Hexa-chlor benzene, CCl_6	Solid	229.0°C.	326°C.
	white needles		
Mono-brom benzene, C_6H_5Br	Liquid	— 31.1°C.	159°C.
Di-brom benzene, C_6H_4 $\begin{matrix} \text{Br} \\ \diagup \\ \text{Br} \end{matrix}$			
o.....	Liquid	— 1.0°C.	224°C.
m.....	Liquid	1.0°C.	220°C.
p.....	Solid	87.0°C.	219°C.
Mono-iodo benzene, C_6H_5I	Liquid	— 29.8°C.	188°C.
Di-iodo benzene, C_6H_4 $\begin{matrix} I \\ \diagup \\ I \end{matrix}$			
o.....	Solid	129.4°C.	285°C.
m.....	Solid	211°C.
p.....	Solid	204°C.

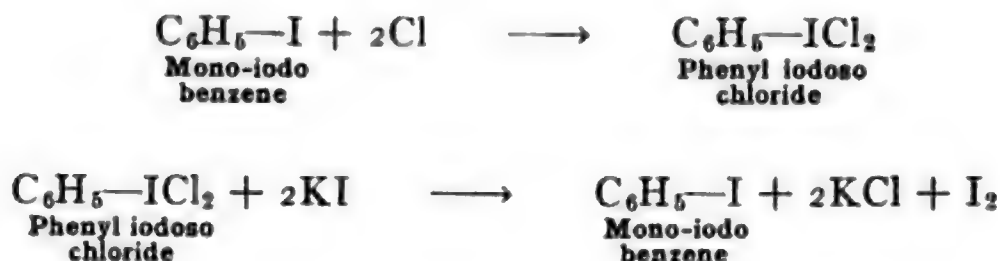
Hexa-chlor benzene is formed by the chlorination not only of benzene itself, but also of other more complex hydrocarbons, *e.g.* **naphthalene**, **anthracene**, **phenanthrene**, **di-phenyl methane** (but not **diphenyl**). Penta-chlor benzene is of interest because it was at one time supposed to exist in isomeric forms which is contrary to the **Kekulé** theory.

Iodo-benzene.—Five of the iodine substitution products of benzene are known, the hexa-iodo benzene having not yet been prepared. The important thing, in connection with the iodo benzenes, is the formation of a group of derivatives not obtained from the corresponding chlorine or bromine products.

Tri-valent and Penta-valent Iodine.—Iodine, it will be recalled, forms compounds in which it acts either as *tri-valent* or *penta-valent*, *e.g.* ICl_3 , ICl_5 , I_2O_3 , I_2O_5 .

Iodo Benzene Dichloride or Phenyl Iodoso Chloride.—When chlorine gas is passed through a chloroform solution of **mono-iodo benzene** there is obtained a yellow crystalline compound which has the composition of $C_6H_5-ICl_2$ and is known as **iodo benzene di-chloride** or

phenyl iodoso chloride. It easily decomposes, by means of potassium iodide, and goes back into mono-iodo benzene.



Iodoso Benzene.—If **phenyl iodoso chloride** is treated with potassium hydroxide or water instead of with potassium iodide, the chlorine is replaced by oxygen, and we obtain a new compound, $\text{C}_6\text{H}_5\text{—IO}$, known as **iodoso benzene**.

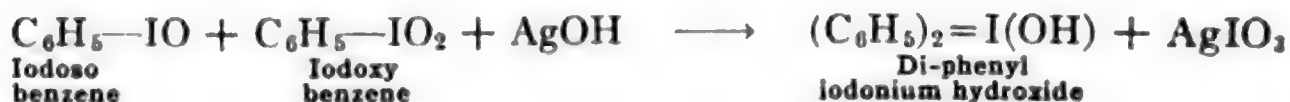


Phenyl Iodonium Hydroxide.—These iodoso compounds are derivatives of the hypothetical base, $\text{C}_6\text{H}_5\text{—I(OH)}_2$, **phenyl iodonium hydroxide**. When a solution of iodoso benzene is heated it decomposes as follows:

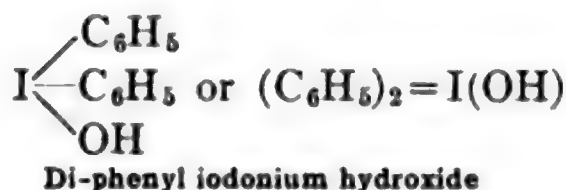


Iodoxy Benzene.—The reaction consists in a reciprocal oxidation and reduction of two molecules of the iodoso benzene. One product is iodo benzene, the other, viz., $\text{C}_6\text{H}_5\text{—IO}_2$, in which the iodine is *penta-valent*, is known as **iodoxy benzene**.

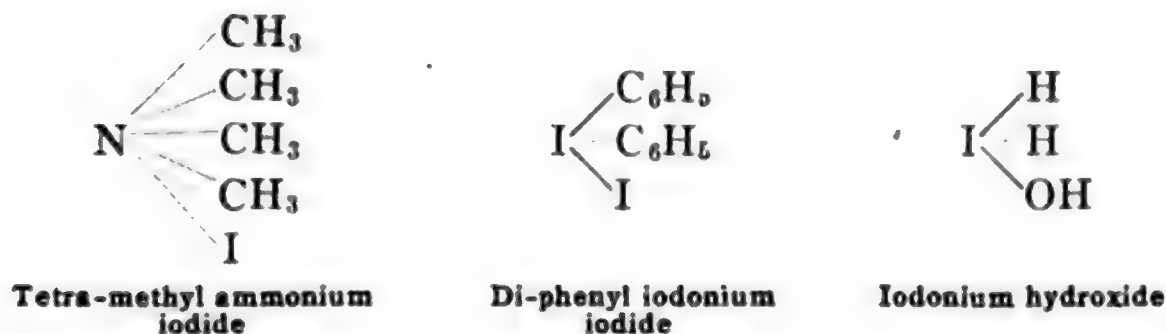
Di-phenyl Iodonium Hydroxide.—When **iodoso benzene** and **iodoxy benzene**, mixed in molecular proportions, are treated with silver hydroxide a strongly basic hydroxide compound is obtained of the formula $(\text{C}_6\text{H}_5)_2=\text{I(OH)}$, known as **di-phenyl iodonium hydroxide**.



The constitution of this compound may be represented by the formula



With potassium iodide it yields the corresponding iodide $(\text{C}_6\text{H}_5)_2 = \text{I—I}$, **di-phenyl iodonium iodide**, which is analogous to the quaternary **tetra-methyl ammonium iodide**.



Iodonium Hydroxide.—These iodonium compounds are considered as derivatives of a hypothetical base, $\text{H}_2\text{I}(\text{OH})$, **iodonium hydroxide**, as above.

HALOGEN SUBSTITUTION PRODUCTS OF BENZENE HOMOLOGUES

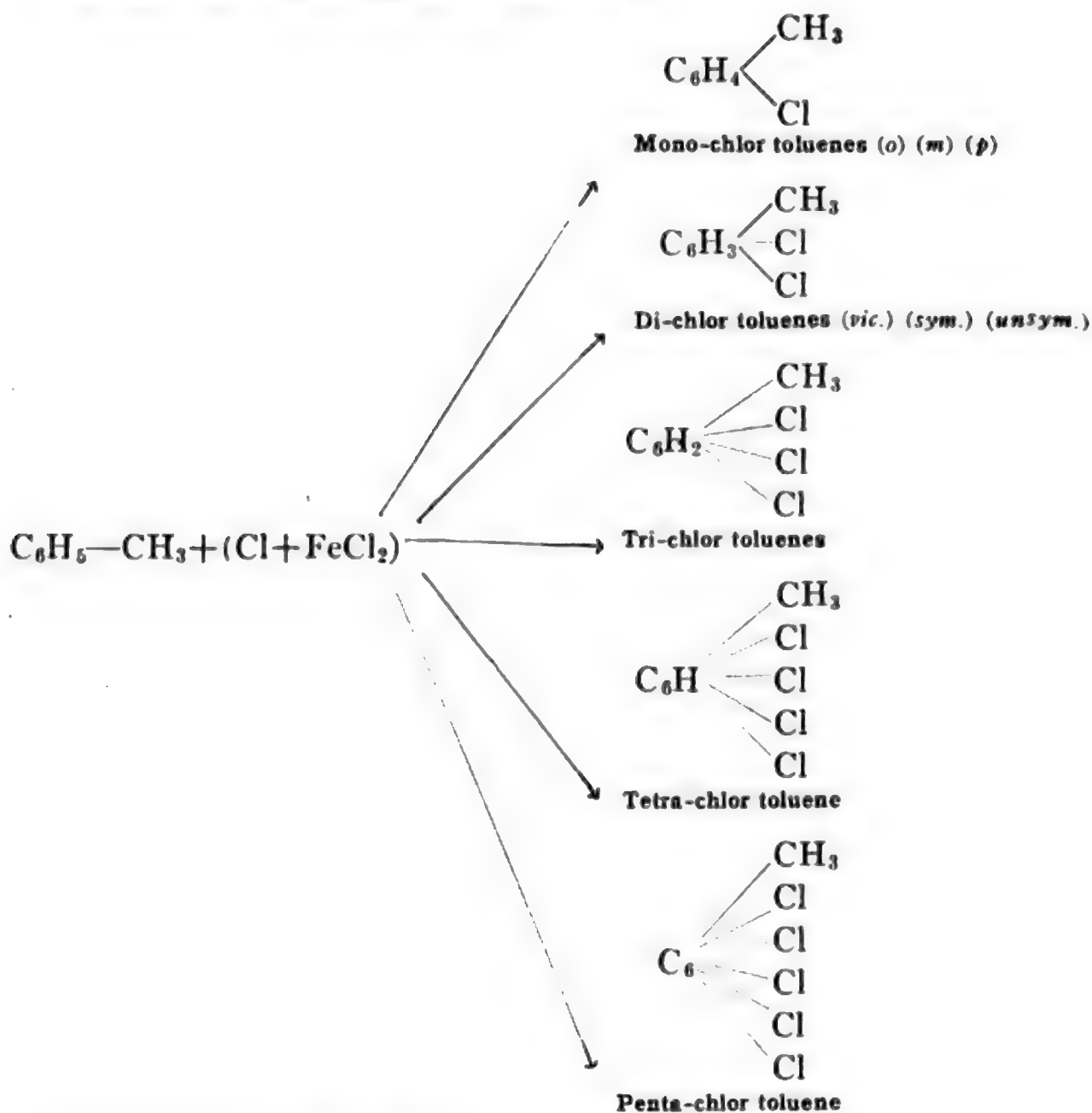
The homologues of benzene are substitution products of benzene in which an aliphatic radical or open chain group is substituted in the ring. They may be represented by the general formula $\text{C}_6\text{H}_6 - \text{xR}_\text{x}$.

Each homologous hydrocarbon, therefore, consists of two distinct parts, viz., the *benzene ring* and the *open chain radical*; each part possessing the characteristic properties belonging to it. By appropriate reactions substitution may be effected in either one or both.

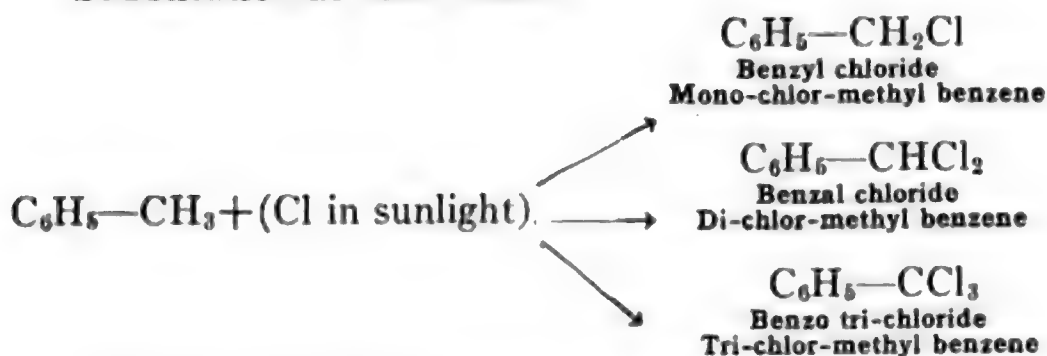
Substitution in Ring, Substitution in Side Chain.—If the substitution of halogens is brought about through the agency of *carriers* the halogen enters the *ring*, but if it occurs in *direct sunlight* or at *boiling temperature* then the halogen enters the *side chain*.

Chlorine Substitution Products of Toluene.—Taking toluene, the first of the benzene homologues, as an illustration we have the following possible mono-chlorine substitution products, all of which are known.

Substitution in Ring, Chlor Toluenes.—



Substitution in Side Chain.

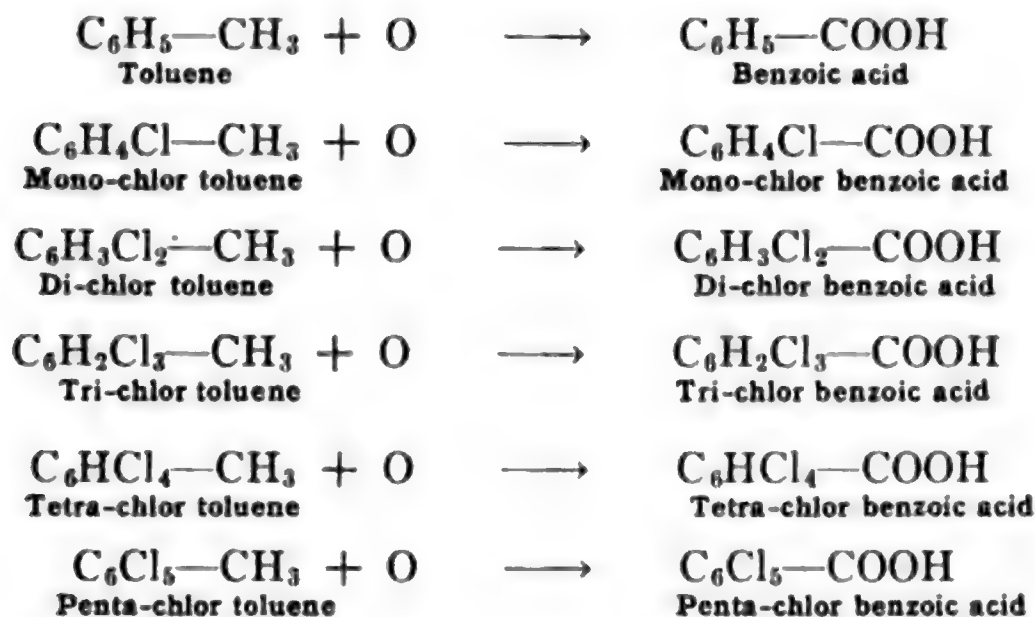


Oxidation Products of Substituted Toluenes.—The oxidation products of these two groups of compounds are distinctly different. We

have spoken of the fact that when toluene itself is oxidized the methyl group becomes converted into carboxyl, the result being mono-carboxy benzene or **benzoic acid**.



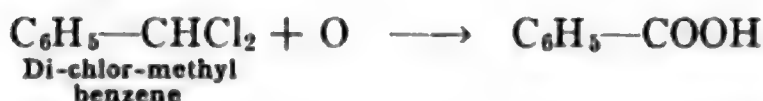
Chlor Toluenes Yield Chlor Benzoic Acids.—The five chlorine substitution products in the first group are made by the action of chlorine in presence of a carrier, the reaction for introducing halogens into the benzene ring. All five of these compounds on oxidation *yield* a *mono-carboxyl* substitution product of benzene, in which there is also substituted in the benzene ring one, two, three, four or five chlorine atoms. This shows that in these compounds the chlorine has entered the ring leaving the side chain, *methyl*, intact, which, by oxidation, yields carboxyl. The products are, therefore, *mono-chlor* to *penta-chlor* benzoic acids.



These chlorine substitution products of toluene are known as **chlor-toluenes** because all of them still have the toluene character, *i.e.* a benzene ring in which one hydrogen is substituted by methyl.

Side Chain Substitution Products Yield Benzoic Acid.—On oxidation the second group of chlorine products, made by substituting chlorine directly in sunlight without use of a carrier, all yield the same product, *viz.*, **benzoic acid** or **mono-carboxy benzene**. This means that in them the benzene ring remains intact and the side chain only is affected by the oxidation. As all of the chlorine is also removed by the oxidation it all must have been in the side chain. They are known,

therefore, as **mono-chlor-methyl**, **di-chlor-methyl** and **tri-chlor-methyl benzenes**, all being *mono-substituted benzenes*.



Because, as we shall see later, the **mono-chlor-methyl benzene** yields benzyl alcohol it is known as **benzyl chloride**. The **di-chlor-methyl benzene** similarly yields **benzaldehyde**, and is, therefore, called **benzal chloride**, and the third is also called **benzo tri-chloride**.

We referred to the fact that substitution in the benzene ring takes place more easily with toluene than with benzene itself, *i.e.*, the presence of a substituted methyl group increases the ease of further substitution in the ring. Also oxidation takes place more easily when substitution has already occurred and still more easily if the side chain is likewise substituted.

Isomerism.—As all of the second group, in which substitution occurs in the side chain, considered as benzene derivatives, are mono-substituted benzenes, they do not exist in isomeric forms, and only one compound of each formula is known. The first group, however, in which halogen substitution occurs in the ring, are all poly-substitution products of benzene, since toluene itself is a mono-substituted benzene. Mono-chlor toluene is, therefore, a di-substituted benzene, and occurs in the three forms, as follows:

ortho-Chlor toluene or 1-Methyl 2-chlor benzene.

meta-Chlor toluene or 1-Methyl 3-chlor benzene.

para-Chlor toluene or 1-Methyl 4-chlor benzene.

By the ordinary chlorination of toluene in presence of a carrier the **ortho** (1-2) and **para** (1-4) products are formed. **Di-chlor toluene**, in the

same way being a *tri-substituted* benzene, occurs in the three forms, *vicinal*, *unsymmetrical* and *symmetrical*, *e.g.*

1-Methyl 2-3-di-chlor benzene.

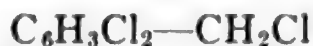
1-Methyl 3-4-di-chlor benzene.

1-Methyl 3-5-di-chlor benzene.

Isomerism of the *tri*- and *tetra*- substituted toluenes will not be considered at length. The chlorine substitution products in which more than one chlorine is substituted may likewise occur in still another isomeric form. Instead of the two chlorines or other substituting elements or groups both entering the ring or the side chain, we may have compounds in which one or more elements enter one position, and at the same time, one or more enter the other position. Such compounds are known, but will simply be mentioned by formula, *e.g.*



1-Chlor-methyl 2-chlor benzene



1-Chlor-methyl 2-3-di-chlor benzene



1-Di-chlor-methyl 2-chlor benzene

Halogen Substitution Products of Higher Homologues.—The halogen substitution products of the homologues of benzene above toluene, *viz.*, **xylene**, **mesitylene**, etc., need not be discussed further than simply to mention them. Of the xylenes, the **para-xylene** is the only one yielding satisfactory halogen products. As only one **mono-chlor para-xylene** is possible, in which the halogen enters the ring, it must have the constitution **1-4-di-methyl 2-chlor benzene**. In the case of **mesitylene** also there is only one mono-halogen product, *e.g.* **1-3-5-tri-methyl 2-iodo benzene**. **Pseudocumene**, which is the **1-3-4-tri-methyl benzene**, yields on chlorination by carriers a mixture of three isomeric products.

1-3-4-Tri-methyl 2-chlor benzene.

1-3-4-Tri-methyl 5-chlor benzene.

1-3-4-Tri-methyl 6-chlor benzene.

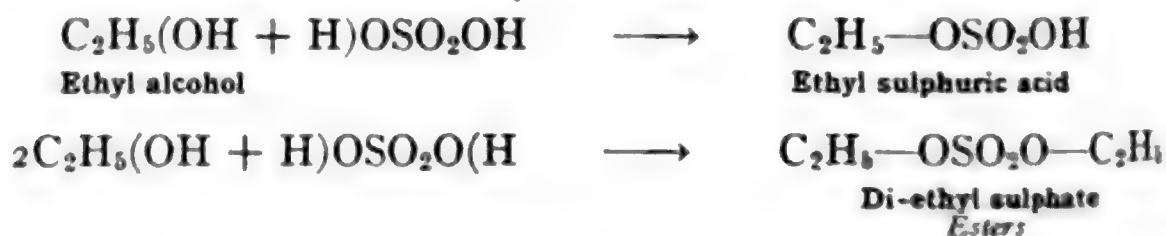
Halogen substitution products of the hydrocarbons containing unsaturated side chains are also known, *e.g.* **chlor styrene**, $\text{C}_6\text{H}_5-\text{CH}=\text{CHCl}$, **phenyl ethylenyl chloride** and **iodo phenyl acetylene**, $\text{C}_6\text{H}_5-\text{C}\equiv\text{CI}$, **phenyl acetylenyl iodide**.

II. SULPHURIC AND SULPHUROUS ACID DERIVATIVES

SULPHONIC ACIDS

Sulphuric Acid Derivatives.—In the aliphatic series we considered the hydroxyl derivatives immediately following the halogen derivatives because in that series the hydroxyl compounds are directly and easily prepared from the halogen substitution products by the action of silver hydroxide, AgOH, or sodium hydroxide, NaOH. In the benzene series the halogen derivatives are followed by the *sulphuric acid derivatives* because, in the first place, the halogen derivatives are not converted into hydroxyl compounds by treatment with silver hydroxide, and in the second place, because the sulphuric acid derivatives of the benzene hydrocarbons are easily formed directly from the hydrocarbons by action of sulphuric acid, which was not the case in the aliphatic series, and because they are exceedingly important as they are readily transformed into other classes of compounds, *e.g.* hydroxyl compounds, *phenols*.

Esters.—It will be recalled that in the aliphatic series there are two classes of derivatives of sulphuric acid. When sulphuric acid reacts with an *alcohol* neutralization takes place between the alcohol, as a base, and the sulphuric acid; water, H—OH, is eliminated and a compound known as an *ethereal salt* or *ester* is obtained.



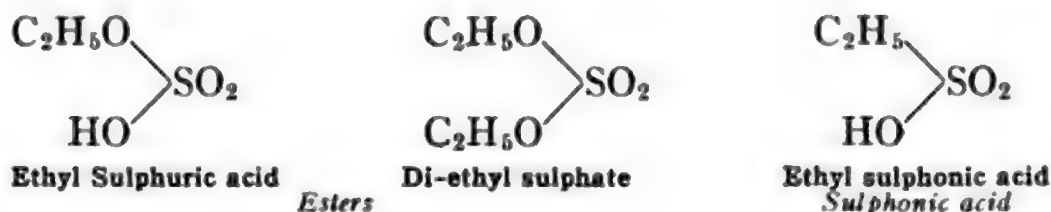
Sulphonic Acids.—When, however, an aliphatic *mercaptan* or *thio-alcohol* is oxidized we obtain a compound, containing a sulphuric acid residue, known as a *sulphonic acid*.



The sulphonic acids are also formed in the aliphatic series by the action of a salt of *sulphurous acid* upon an alkyl halide.



Though these sulphonic acids are isomeric with the esters of sulphurous acid they do not react like esters, *i.e.* they are *not hydrolyzed* by water or alkalies *yielding the alcohol and sulphurous acid*. We, therefore, represent the difference between *esters* and *sulphonic acids* by the following formulas:



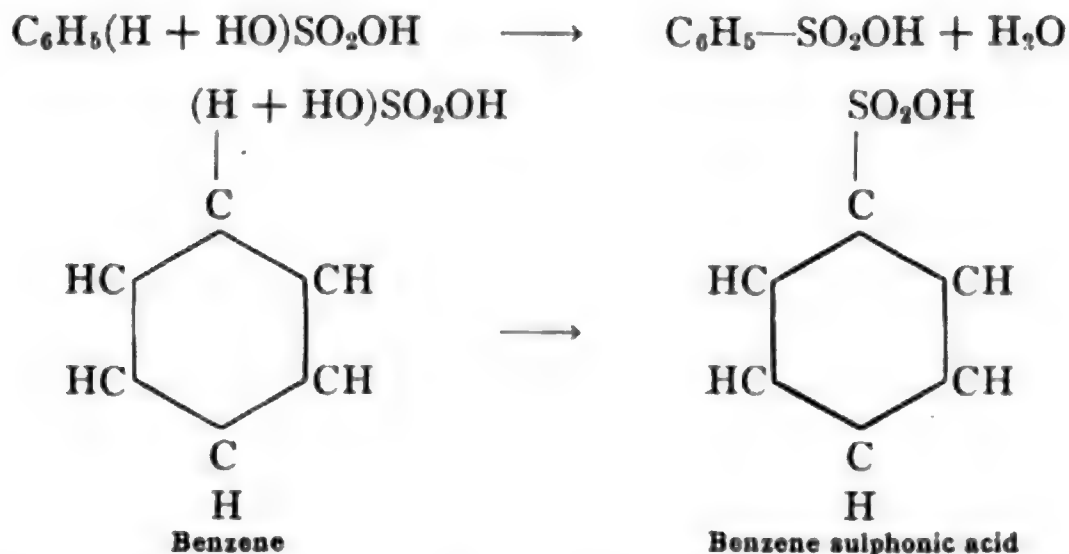
In the case of the ester the hydrocarbon *radical* replaces the *hydroxyl hydrogen* of the sulphuric acid, while in the *sulphonic acid* the *radical* replaces the entire *hydroxyl group* of the acid. In the former the *sulphur* of the acid is *linked* to a *carbon* of the radical *through an oxygen atom*, while in the latter the *sulphur* is *linked directly to carbon*.

The sulphonic acids of the benzene series are exactly analogous to those of the aliphatic series, *i.e.* they are *non-hydrolyzable*, and are represented by the general formula $\text{R—SO}_2\text{—OH}$. The method of preparation of the aliphatic sulphonic acids from the halogen substitution products and a salt of sulphurous acid is not applicable in the benzene series.

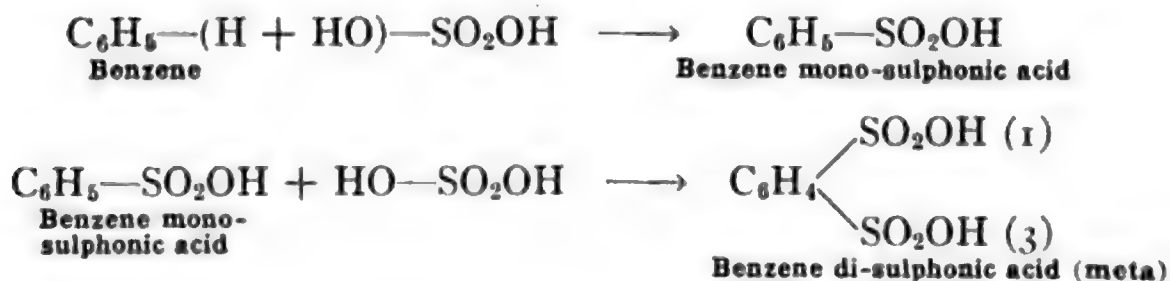
Preparation of Benzene Sulphonic Acids.—The method of preparing benzene sulphonic acids helps to explain and prove their constitution. We have stated that one of the characteristic distinctions between the aliphatic and benzene hydrocarbons is that with the former direct substitution of a nitric or sulphuric acid group does not take place by treatment with the acid itself; whereas with the latter such direct substitution takes place readily.

When benzene or a homologue is treated with concentrated or fuming sulphuric acid the hydrocarbon loses *hydrogen* and the acid

loses *hydroxyl*, water being eliminated, and the *sulphonic acid* of the hydrocarbon is formed.



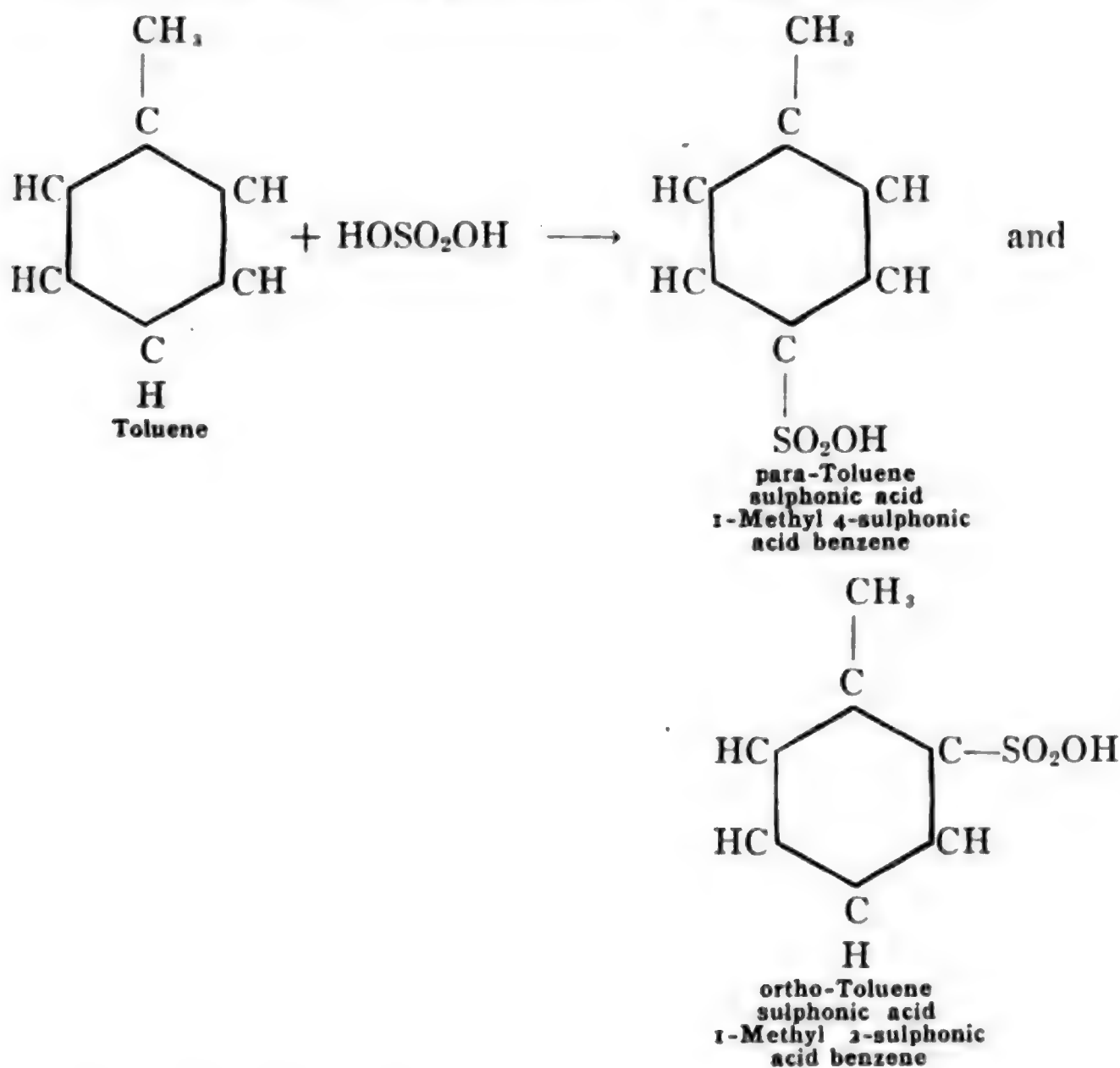
Therefore, in the sulphonic acids, the sulphuric acid residue ($\text{SO}_2\text{—OH}$) is substituted in the ring, the *carbon* of the ring being in *direct union* with the *sulphur* of the acid residue. The sulphonic acids of the benzene series are of great importance while those of the aliphatic series are only slightly so. When benzene is treated with fuming sulphuric acid, or boiled for thirty hours with ordinary concentrated acid, **benzene mono-sulphonic acid** is formed. By further treatment of the mono-sulphonic acid with fuming sulphuric acid the **benzene di-sulphonic acid** is formed which, as stated on page 506, is the *meta* compound.



The *para* or 1-4-di-sulphonic acid of benzene is also known and likewise the 1-3-5-tri-sulphonic acid.

Sulphonic Acids of Benzene Homologues.—The homologues of benzene react in the same way toward sulphuric acid with the difference, already mentioned, that substitution takes place even more easily, due to the presence in the ring of methyl or other aliphatic radicals. Toluene sulphonic acids are, therefore, more easily prepared than benzene sulphonic acid.

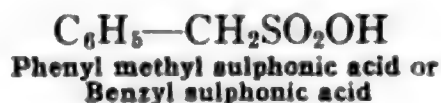
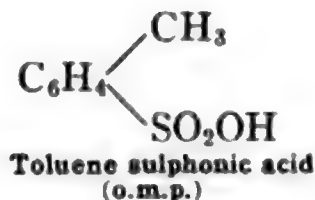
Toluene Sulphonic Acids, para and ortho.—With the methyl group already substituted in the benzene ring the sulphonic acid group enters the *para* and *ortho* positions in preference to the *meta*. If one sulphonic acid group is substituted a second one enters the position *meta* to the first. These facts are of importance in connection with syntheses to be considered later, e.g. in the preparation of **saccharin** (p. 712).



The *meta* compound is prepared by other methods (p. 532) in which by starting with a toluene derivative, in which the *ortho* and *para* positions are occupied, sulphonation affects the *meta* position. The *ortho* and *para* substituents are then removed. Sulphonic acids of **xylene**, **mesitylene** and **cymene** are also known.

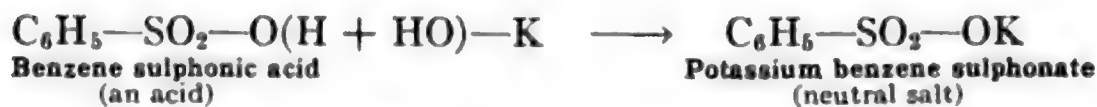
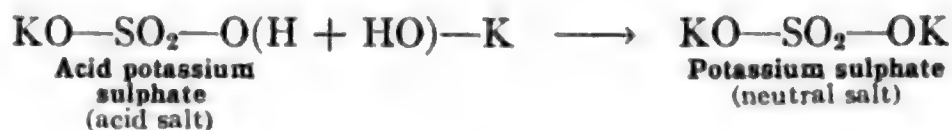
In the case of the homologues of benzene we have two different types of sulphonic acids just as we had of the halogen substitution products, viz., (1) those in which the sulphonic acid group is substituted

in the ring, and (2) those in which it is substituted in the aliphatic side chain.



The former are true aromatic sulphonic acids prepared by direct sulphonation, and reacting like benzene sulphonic acid. The latter are aliphatic sulphonic acids both in methods of preparation and reaction.

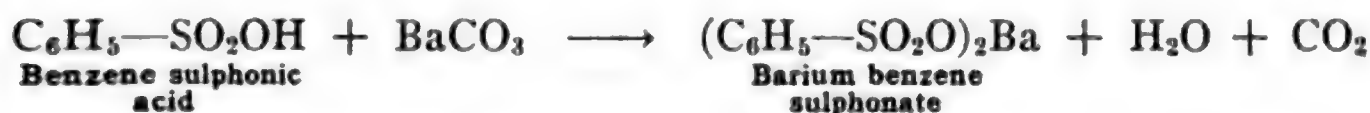
Acid Character.—The sulphonic acids of the benzene hydrocarbons are usually strongly acid, colorless crystalline substances, very easily soluble in water. On this account, in the preparation of dyes in particular, the formation of a sulphonic acid is brought about in order to convert an insoluble hydrocarbon or a derivative into an easily soluble compound. The acidity of benzene sulphonic acid, $\text{C}_6\text{H}_5\text{—SO}_2\text{OH}$, like the acidity of **acid potassium sulphate**, $\text{KO—SO}_2\text{OH}$, and **ethyl sulphuric acid**, $\text{C}_2\text{H}_5\text{O—SO}_2\text{—OH}$, is due to the remaining acid hydrogen of the sulphuric acid. The first, however, is an acid, the second is an acid salt, the third an acid ester. It is extremely important in connection with the sulphonic acids, which form such an essential group of compounds in the benzene series, to get clearly in mind this difference between sulphonic acids and esters or ethereal salts, and the explanation of the acid character of the former. Benzene sulphonic acid is monobasic possessing one-half the acidic properties of the original sulphuric acid. It, therefore, reacts acid to litmus, and is able to form neutral salts with metals by the replacement of the final acid hydrogen with a metal.



The general formula for salts of the sulphonic acids is, therefore, Ring— SO_2 —OM.

Salts of Sulphonic Acids.—The salts of the sulphonic acids, especially those of sodium, potassium, silver, lead, barium and calcium, are

usually crystalline, but not quite so easily soluble as the free acids. Therefore, to obtain pure sulphonic acids it is customary to convert the acid first into some one of these salts, and then to reform the free acid by treatment of the purified salt with sulphuric acid. In the case of the barium, calcium or lead salts the metal is precipitated as an insoluble sulphate.

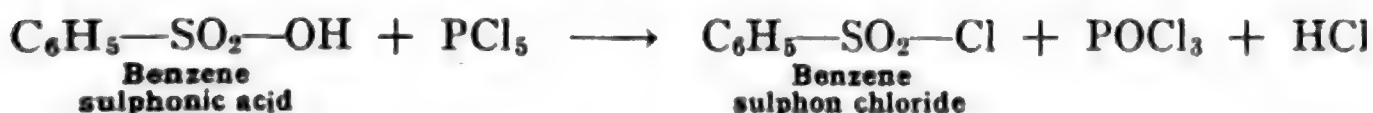


The importance of the sulphonic acids of the benzene series is due to their easy preparation, and to the variety of reactions which they undergo in the formation of other derivatives.

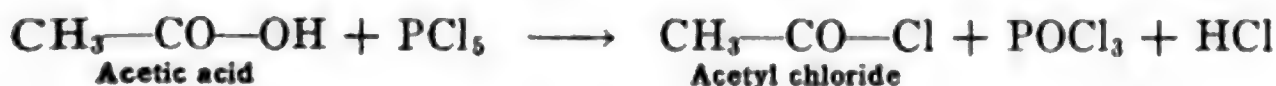
Reactions.—The most important reactions of the sulphonic acids are the following:

(1) *Neutralization* forming salts as already discussed.

Sulphon Chlorides.—(2) *Reaction with phosphorus penta-chloride.* As sulphonic acids contain the acid *hydroxyl* group, they undergo the characteristic reaction with chlorides of phosphorus and exchange the hydroxyl for chlorine. The product is known as a *sulphon chloride*.



This reaction is analogous to that of acetic acid with phosphorus pentachloride by which acetyl chloride is formed.

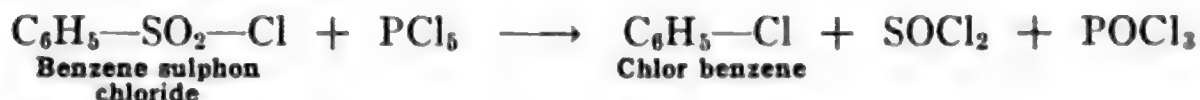


Sulphon Amides.—Just as acetyl chloride is converted into acetamide by the action of ammonia so **benzene sulphon chloride** yields **benzene sulphon amide** by the same treatment.



These two reactions by which a *sulphonic acid* is converted first into the *sulphon chloride* and then into the *sulphon amide* may be applied with considerable ease to all sulphonic acids. The sulphon chloride reacts further with phosphorus penta-chloride; all of the sulphur

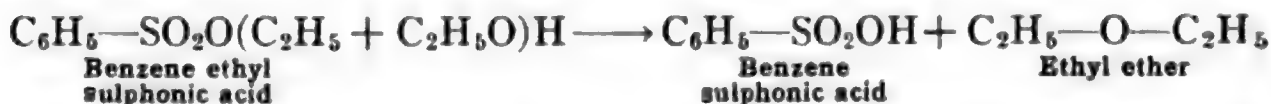
and oxygen are removed, and the halogen substitution product of the hydrocarbon remains.



Esters.—(3) *Reaction with alcohols.* As the sulphonic acids are acid compounds still containing one acid hydroxyl they react with alcohols forming esters.



This benzene ethyl sulphonic acid is analogous to ethyl sulphuric acid, $\text{HOSO}_2\text{OC}_2\text{H}_5$, and as the latter with excess of alcohol yields **ethyl ether** and reforms sulphuric acid so benzene ethyl sulphonic acid with excess alcohol yields ethyl ether and reforms the benzene sulphonic acid.



These reactions of sulphonic acids with phosphorus penta-chloride and with alcohol both prove that in sulphonic acids there is *one*, and *only one*, acid hydroxyl remaining.

Sulphonic Acids to Hydroxyl Compounds.—(4) *Reactions with alkalis by fusion.* In the aliphatic series the most important synthetic reaction for the formation of hydroxyl derivatives is the treatment of the alkyl halides with silver hydroxide, which reaction we have said does not occur in the benzene series when the substitution is in the ring and not in the side chain. The most important method for preparing ring-hydroxyl compounds is by the fusion of a sulphonic acid or its salt with alkalis, potassium or sodium hydroxide, a reaction which does not occur with the aliphatic sulphonic acids.



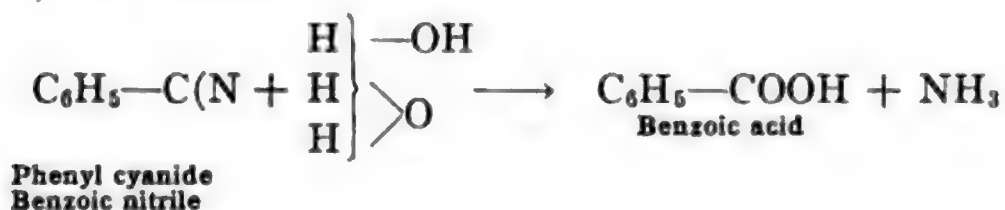
The other product of the reaction is a salt of **sulphurous acid**, which recalls the relation between the aliphatic sulphonic acids and sulphurous acid.



Cyanides or Nitriles.—(5) *Reaction with potassium cyanide.* Entirely analogous to the preceding reaction is that between sulphonic acids and potassium cyanide. When a sulphonic acid is *fused* with **potassium cyanide** the *cyanogen substitution product* of the hydrocarbon is formed



Just as the aliphatic cyanides by hydrolysis yield carboxyl products or acids so the benzene cyanides also yield acids on hydrolysis and are, therefore, *acid nitriles*.

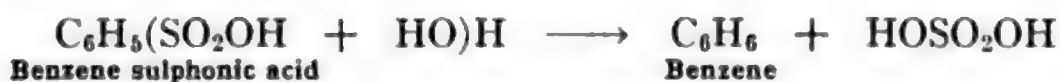


The formation of cyanogen products from the sulphonic acids is of importance, therefore, as a step in the formation of the corresponding acids.

Acids Directly.—(6) *Reaction with sodium formate.* Acids of the benzene series may also be formed directly from the sulphonic acids by treatment with **sodium formate**.

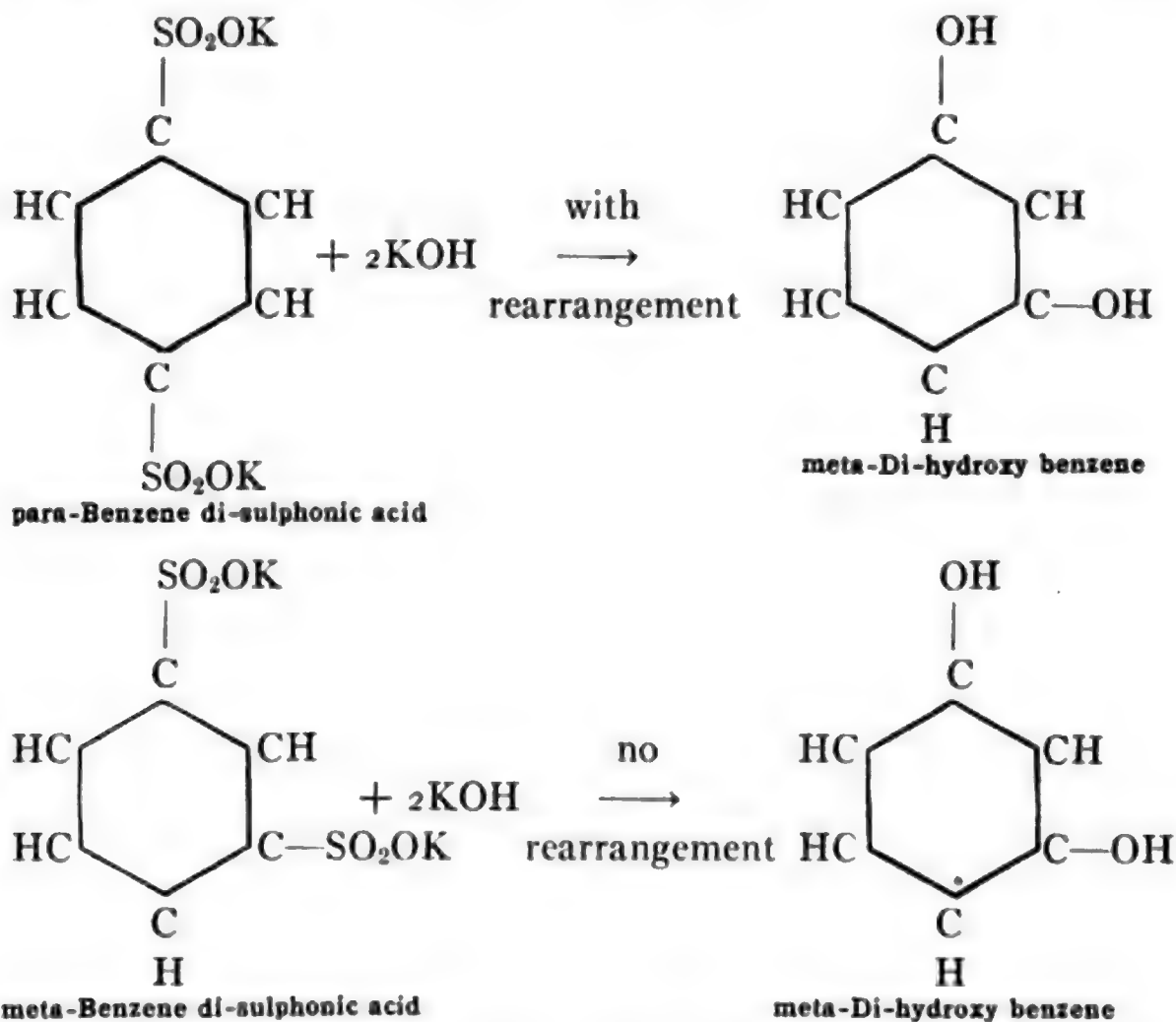


Hydrolysis.—(7) *Reaction with water, hydrolysis.* As we have stated in discussing the relation between sulphonic acids and sulphuric acid esters the former do not hydrolyze as do the latter, yielding the acid and alcohol. Hydrolysis may, however, be brought about by the use of steam and the products of such reaction are the *hydrocarbon* and sulphuric acid.



The reaction is useful in preparing pure hydrocarbons as in the case of the three isomeric xylenes. The above reactions have been written in all cases with the free acid, but in practice a salt, usually potassium or sodium, is used. The reactions then are identical only the potassium or sodium salt of the other product is formed.

Reactions of Di-sulphonic Acids.—The *di-sulphonic* acids and *tri-sulphonic acids* react exactly as do the *mono-sulphonic* acids yielding the corresponding *di* and *tri*-products. In the case of the di-sulphonic acids, however, which occur of course as *ortho*, *meta* and *para* compounds, there are interesting rearrangements which take place so that a di-sulphonic acid does not *always* yield a product with the substituting groups in the original positions. When *para*-di-sulphonic acid of benzene is fused with potassium hydroxide the di-hydroxyl product is obtained (reaction 3), but instead of being the *para* compound it is the *meta*. The *meta* di-sulphonic acid of benzene by similar treatment undergoes no rearrangement and the *meta* compound is also obtained.



In a similar way the formation of *di-carboxyl* derivatives from the *di-cyanogen products* (reaction 4) is subject to a like rearrangement in the position of the substituting groups; *but* the *direct conversion* of *di-sulphonic acids* into *di-carboxyl acids* by treatment with *sodium formate* (reaction 5) does *not* undergo any rearrangement. As will be under-

stood, these facts are of great importance in the synthesis of di-substitution products.

Summary.—Bringing together the reactions of sulphonic acids as we have given them we see that either directly or indirectly they are capable of transformation into the following compounds:

Sulphonic acids, *e.g.* $\text{C}_6\text{H}_5\text{—SO}_2\text{—OH}$, may be converted into:

Salts (sulphonates) by neutralization,	$\text{C}_6\text{H}_5\text{—SO}_2\text{—OK}$
Sulphon chlorides, by PCl_5 ,	$\text{C}_6\text{H}_5\text{—SO}_2\text{—Cl}$
Sulphon amides, from the chloride by NH_3 ,	$\text{C}_6\text{H}_5\text{—SO}_2\text{—NH}_2$
Esters, by alcohols,	$\text{C}_6\text{H}_5\text{—SO}_2\text{—OC}_2\text{H}_5$
Ring hydroxyl compounds, by alkali fusion,	$\text{C}_6\text{H}_5\text{—OH}$
Cyanogen compounds (nitriles), by KCN fusion,	$\text{C}_6\text{H}_5\text{—CN}$
Acids, by H—COONa , or from nitriles by hydrolysis,	$\text{C}_6\text{H}_5\text{—COOH}$
Hydrocarbons, by steam,	C_6H_6

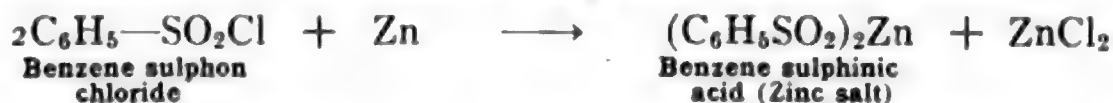
SULPHINIC ACIDS

Sulphurous Acid Derivatives.—Just as we have the two acids of sulphur, *sulphuric* and *sulphurous*, differing from each other by the amount of oxygen present, so we have benzene derivatives of sulphurous acid corresponding to the sulphuric acid derivatives, but containing *one atom of oxygen less*.

Sulphinic Acids.—These sulphurous acid derivatives are known as *sulphinic acids* in distinction from *sulphonic acids*.



As sulphuric acid by reduction yields sulphurous acid so the *sulphonic acids* by reduction yield *sulphinic acids*. The action takes place better, however, if instead of a sulphon acid we use the corresponding *sulphon chloride*. When **benzene sulphon chloride** is treated with zinc the zinc salt of the **benzene sulphinic acid** is obtained.



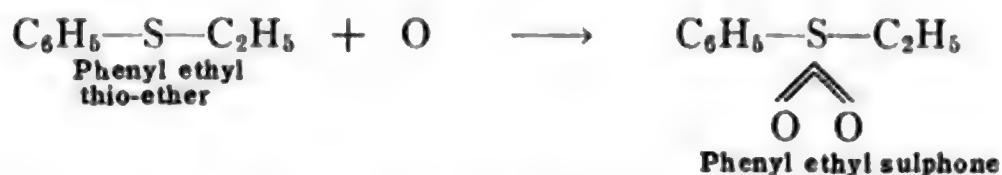
The free acid is prepared by the action of **sulphurous anhydride** upon **benzene**



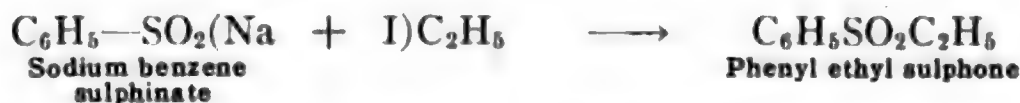
The sulphinic acids are of special interest because of a phenomenon known as *desmotropism* which exists in these compounds. When the

thio ether or sulphide containing a benzene radical and an aliphatic radical, *e.g.* $\text{C}_6\text{H}_5\text{—S—C}_2\text{H}_5$, **phenyl ethyl thio-ether** or **phenyl ethyl sulphide**, is oxidized we obtain a compound known as a *sulphone*.

Sulphones.



In this compound both radicals are considered as united directly to the sulphur. When a salt of **benzene sulphinic acid** is treated with an alkyl halide a reaction resembling the **Fittig** and **Wurtz** reactions takes place.



The product is identical with that obtained from the thio-ether, *i.e.*, a *sulphone*.

Formula for Sulphinic Acids.—From this it would appear that the formula for the sodium salt of benzene sulphinic acid is $\text{C}_6\text{H}_5\text{—S—Na}$



and the free acid, $\text{C}_6\text{H}_5\text{—S—H}$, and not $\text{C}_6\text{H}_5\text{—S—OH}$ as we should



expect if it is analogous to the sulphonic acids $\text{C}_6\text{H}_5\text{—S—OH}$. In

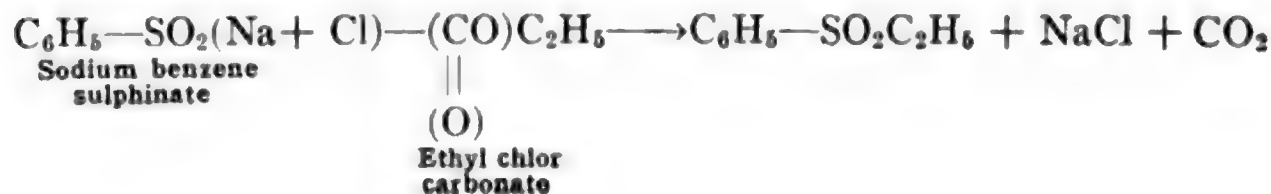


such a compound the *acid hydrogen* is *not hydroxyl hydrogen*, but is linked *directly* to the sulphur.

If, however, a sulphinic acid salt is treated with **ethyl chlor carbonate**, which is $\text{C}_2\text{H}_5\text{O—C—Cl}$, the elimination of NaCl and CO_2 takes place



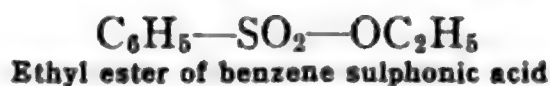
and we obtain a compound of the same composition as the sulphone, but which is distinctly different.



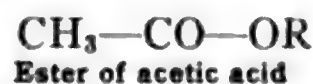
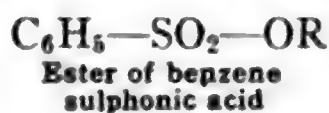
Sulphinic Acid Ester.—This compound is readily *hydrolyzed* yielding *ethyl alcohol*. It must be, therefore, a true ester of sulphinic acid, and must be represented by the formula



Also this compound on oxidation yields a true ester of sulphonic acid



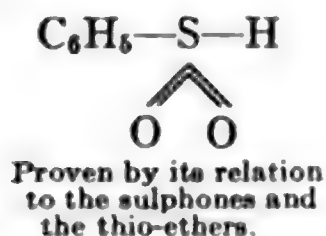
In all esters of oxygen acids a radical must be linked to an oxygen, it having replaced a hydroxyl hydrogen in an acid, *e.g.*



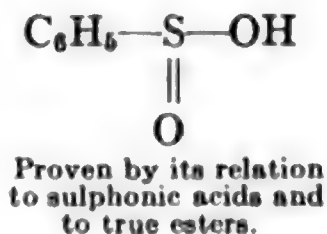
According then to these reactions the formula of the **benzene sulphinic acid** is exactly analogous to that of benzene sulphonic acid, *i.e.*,



We have then two constitutions for sulphinic acid and its salts, each one of which is proven by definite reactions.



Benzene Sulphinic Acid
Desmotropic Forms



Desmotropism.—Such a phenomenon of a single *non-isomeric* compound giving definite evidence of existence in *two* forms is known as *desmotropism*.

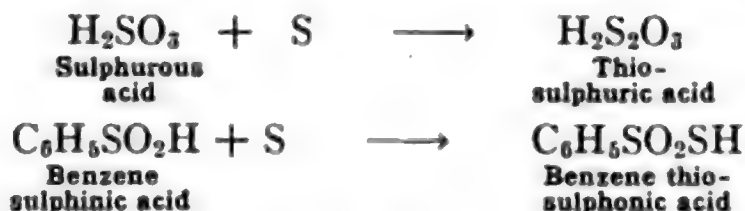
Thio-sulphonic Acids.—Thio-sulphuric acid is related to sulphuric in having an oxygen of the latter replaced by sulphur.



In exactly the same relationship stand the thio-sulphonic acids to the sulphonic acids.



As thiosulphates are made by treating sulphites with sulphur so thiosulphonic acids result when *sulphinic acids* are treated with sulphur.

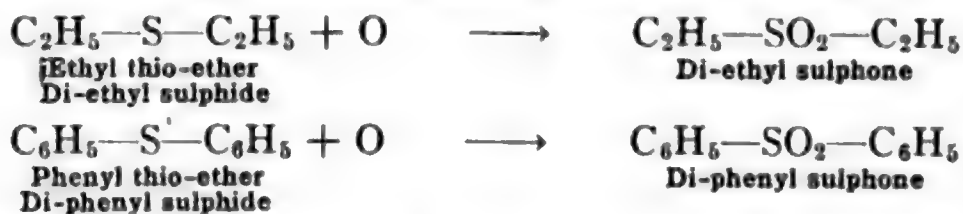


Salts of thio-sulphonic acids are also prepared by treating *sulphon chlorides* with metallic *sulphides*, e.g. K_2S .

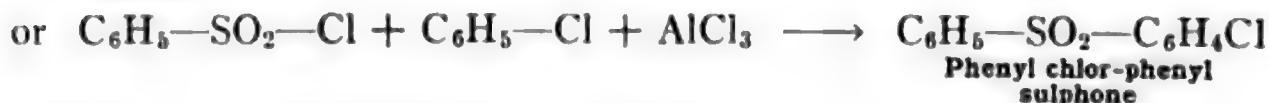


SULPHONES

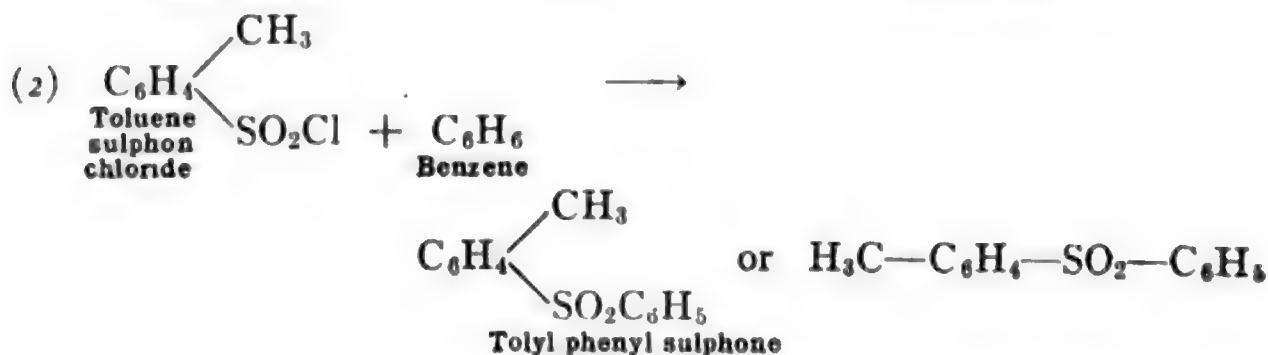
Synthesis of Sulphones.—As previously discussed, these compounds are direct oxidation products of the sulphides or thio-ethers.



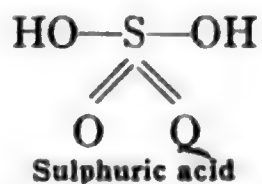
They may also be made from sulphon chlorides by treating with a hydrocarbon or a halogen derivative, in the presence of AlCl_3 .



By means of this last reaction and using in one case **benzene sulphon chloride** and **toluene**, and in the second case **toluene sulphon chloride** and **benzene**, exactly the *same* **phenyl tolyl sulphone** is formed.



This means that in sulphuric acid the two hydroxyl groups are exactly the same, for whichever one is replaced by chlorine and then by a hydrocarbon radical the resulting compound is the same. Therefore sulphuric acid must be

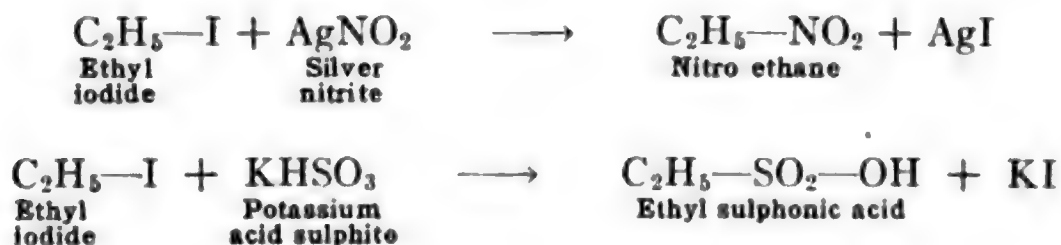


III. NITRIC AND NITROUS ACID DERIVATIVES

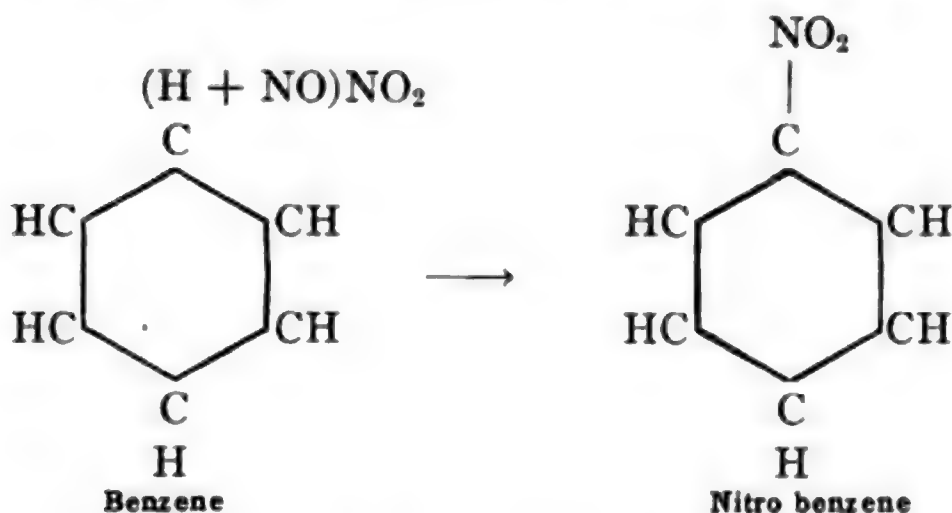
NITRO COMPOUNDS

In the same way in which we have derivatives of the hydrocarbons containing either sulphuric acid or sulphurous acid groups so also we have derivatives containing either of the nitrogen acid groups, *i.e.* **nitric acid**, HNO_3 , and **nitrous acid**, HNO_2 . As in the case of the corresponding aliphatic derivatives, the two classes of compounds are known respectively as *nitro compounds*, and *nitroso compounds*.

The aliphatic nitro compounds are prepared by treating an alkyl halide with **silver nitrite**, AgNO_2 , analogous to the preparation of the sulphonic acids by treating an alkyl halide with potassium acid sulphite, KHSO_3 . This relation, between the organic derivatives of sulphuric and nitric acids and the salts of the sulphur and nitrogen acids poorer in oxygen, is very important.



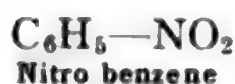
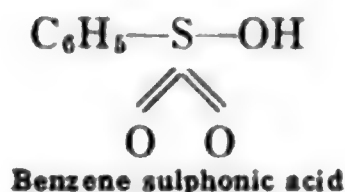
In the benzene series the nitric acid derivatives, like the sulphuric acid derivatives, are not prepared by this reaction with the salts of the oxygen poorer acid, but are easily made by direct treatment of the hydrocarbon with the acid. This direct sulphonation and nitration of the benzene hydrocarbons, remember, is one of the characteristic differences between them and their aliphatic relatives. When benzene is treated with concentrated nitric acid or fuming nitric acid, in the presence of sulphuric acid, one or more nitric acid groups enter the benzene ring. The reaction is exactly similar to the sulphonation of a hydrocarbon, *viz.*, hydrogen from the hydrocarbon and hydroxyl from the acid are eliminated as water, and the acid group enters the ring in place of the hydrogen.



The sulphonic acids, it will be recalled, are strong acids, their acid character being due to the remaining acid hydroxyl left in the compound. Sulphuric acid is di-basic and only *one* of the two hydroxyls is eliminated by the substitution in the ring. Nitric acid, however, is mono-basic and possesses only one acid hydroxyl.

Not Acids.—When, therefore, this hydroxyl is removed by the reaction of nitration the residue contains no remaining acid hydroxyl and the compound can not be acid. **Nitro benzene** and the other nitro compounds of this series are unlike the sulphonic acids then in that they are neutral compounds.

Not Esters, Non-hydrolyzable.—The nitro compounds resemble the sulphonic acids, however, in that they are non-hydrolyzable, and, therefore, are not esters. In them the benzene ring is linked *directly to the nitrogen*; as in the sulphonic acids the ring is linked directly to the sulphur.



Nitro benzene can be heated with water for a long time at 200° without decomposition.

Reduction.—Another reaction of the nitro compounds which proves that the nitrogen is directly linked to the ring is their reduction to *ammonia derivatives*. As will be explained more fully when we take up the ammonia derivatives, just as nitric acid by complete reduction yields ammonia, so nitro benzene and other nitro compounds are

reduced to compounds in which an ammonia residue is substituted in the ring, the nitrogen being directly linked to the carbon. The nitrogen in the nitro compounds must then also be directly linked to the carbon of the ring.



Di- and Tri-nitro Products.—By intensifying the action of nitration (by heat or fuming nitric acid) more than one nitro group is substituted in the ring, and *di*- and *tri*-nitro derivatives of the hydrocarbons result. In the formation of the di-substitution products of benzene the second nitro group enters the *meta* position.

Homologous Nitro Compounds.—When the nitration of the benzene homologues is effected by direct action of the acid, as in the case of benzene, the nitro group enters the ring. In the case of toluene it takes the *para* and *ortho* positions. If the nitro group is substituted in the side chain it is introduced by the reactions characteristic of the aliphatic nitro compounds, *i.e.* by the action of silver nitrite upon a halide.

Nitro Benzenes

Mono-nitro Benzene.—When benzene is treated with concentrated nitric and sulphuric acids at ordinary temperatures, or only moderate heat, only *one* nitro group is substituted and **mono-nitro benzene** is the product. If different proportions of the two acids be used, or if fuming nitric acid be added and the mixture boiled, then two nitro groups are substituted, and **di-nitro benzene** results.

Mono-nitro benzene is a pale yellow liquid heavier than water; sp. gr. 1.2; boiling point 209.4°; melting point +3°. It distils with water vapor and is soluble in alcohol. It is known as *oil of mirbane*, but because of its resemblance in odor to oil of bitter almonds it is used as a substitute for the latter in perfumes. The chief importance of the compound is due to its easy preparation and its transformation by reduction into **amino benzene** or **aniline**, through which it becomes the starting point in the manufacture of dyes.

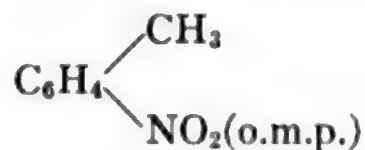
Di-nitro Benzene.—Of the three isomeric di-nitro benzenes the *meta* is the one formed by direct nitration with fuming nitric acid. The proof of its *meta* constitution is its transformation into **meta xylene**.

It will be recalled that the formation of the di-brom benzene resulted in the *para* and *ortho* compounds and no *meta*; whereas the di-nitro benzene formed is the *meta* only. **meta-Di-nitro benzene** is a solid crystalline substance of pale yellow color, the crystals being fine needles; melting point 90° . The *ortho* and *para* di-nitro benzenes have been prepared by other reactions.

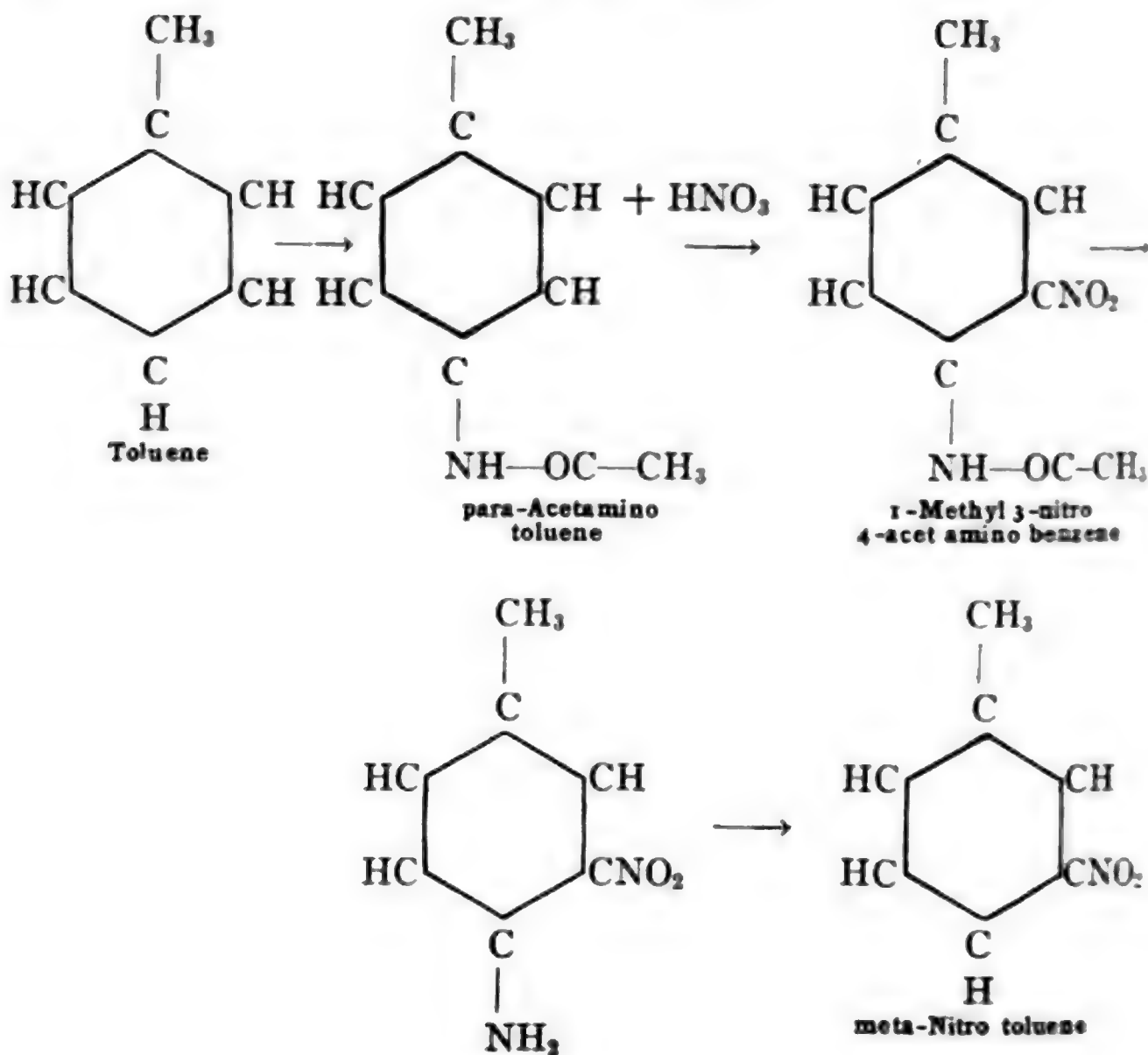
Tri-nitro Benzenes.—Of the three isomeric tri-nitro benzenes the symmetrical or 1-3-5 compound is the one formed by intense direct nitration of benzene. The 1-2-4 compound has been made by further nitration of **para-di-nitro benzene**.

Nitro Toluenes

The mono-nitro toluenes, like the mono-chlor toluenes being di-substituted benzenes, are known in the three isomeric forms,



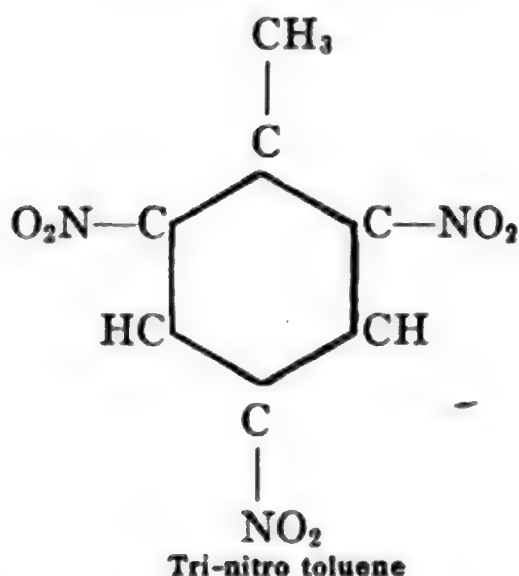
Whereas when a second nitro group enters a benzene ring in which there is one already present it takes the *meta* position; a nitro group entering a ring in which one methyl group is already substituted takes the *para* and *ortho* positions and not the *meta*. Therefore, as was previously discussed (p. 506), the formation of *ortho*, *meta* or *para* disubstitution products of benzene depends on the character of the first group substituted rather than the second. In cases when one isomer is not formed by direct action we can obtain it by an indirect process. If, for instance, we desire the *meta* compound, when by the direct reaction the *para* compound is formed, we proceed by first occupying the *para* position with a substituting group which may afterwards be converted back to hydrogen. Then by direct substitution of the desired group, entrance will be effected in the position *meta* to the first group. For example, direct action of nitric acid on toluene results in **para-nitro toluene**. If the following reactions are followed the **meta-nitro toluene** may be obtained,



By following a similar plan any desired product may be obtained.

The nitro toluenes are of like importance to nitro benzene as the starting point in the preparation of valuable dyes of the aniline or substituted ammonia group.

Tri-nitro Toluene. T.N.T.—One of the nitro toluenes is of especial interest and importance because of its use as a military high explosive. This is **tri-nitro toluene**, commonly known as **T.N.T.** Other names also used for the substance are, *trotyl*, *trinol*, *trilite* and *tritol*. The constitution of the compound is that of the symmetrical or **2-4-6-tri-nitro toluene**. As a benzene derivative it is, therefore, **1-methyl 2-4-6-tri-nitro benzene**.



The fact that strong nitration of toluene results in this particular isomer is in accord with the general rule that a substituting group in the benzene ring which already has a methyl group substituted in it takes the *para* or the *ortho* position. Thus if three nitro groups enter the ring of toluene they should take the two *ortho* and the one *para* position to the methyl, *i.e.* the 2-4-6 positions.

The compound is made by strong nitration of toluene by means of nitric and sulphuric acids. Usually the *para*- and *ortho*-mono-nitro toluenes are first prepared by a mild nitration with nitric acid alone. The *para* compound being in the excess is then separated and used as the starting point for making the tri-nitro compound. One hundred parts of **para-mono-nitro toluene** are then treated at 60°–65° with a mixture of 75 parts of nitric acid of 91–92 per cent and 150 parts of sulphuric acid of 95–96 per cent. The mixed acid is added slowly while the warm toluene is stirred. The resulting mixture is heated to 80° for one half hour and then allowed to cool. The crystalline product, which is **ortho-para-di-nitro toluene**, or *1-methyl 2-4-di-nitro benzene*, m.p. 69.5°, is then separated from the excess acid. The di-nitro toluene is dissolved by gently heating in four times its weight of sulphuric acid of 95–96 per cent. Nitric acid of 90–92 per cent is then added in an amount equal to one and one-half times the weight of the di-nitro toluene, the mixture being kept cool. Digestion at 90°–95° with occasional stirring then follows for four or five hours until the evolution of gases ceases. The product is then cooled and the excess acid separated from the crystalline mass which is washed with hot water and very dilute sodium hydroxide. On cooling to 70° the mass solidifies and is used without further purification. The yield is 150 parts of

tri-nitro toluene from 100 parts of **di-nitro toluene**. It is somewhat poisonous and when recrystallized from hot alcohol it forms white crystals melting at 81.5° .

Tri-nitro toluene cannot be exploded by a flame nor by heating in the open, and is only slightly decomposed by striking it a blow. It is best exploded by means of a detonator of fulminate of mercury. It is used for military purposes in shells, bombs and submarine mines. It also forms a constituent of many mixed explosives. It is about 5 per cent less powerful and also less violent and less sensitive than **picric acid** (p. 630), and does not form sensitive salts or other products under storage conditions as does the latter. A few examples may be given of mixed explosives made with tri-nitro toluene in which **ammonium nitrate** is used as an oxidizer. The presence of the nitrate weakens the power of the T.N.T., but the mixtures are not very sensitive and are adapted to military purposes and some of them to mine blasting.

Amatol is such a mixed explosive and is used very largely for shells. It has varying proportions of the two substances; *e.g.*, amatol 40/60 means 40 per cent ammonium nitrate and 60 per cent T.N.T.

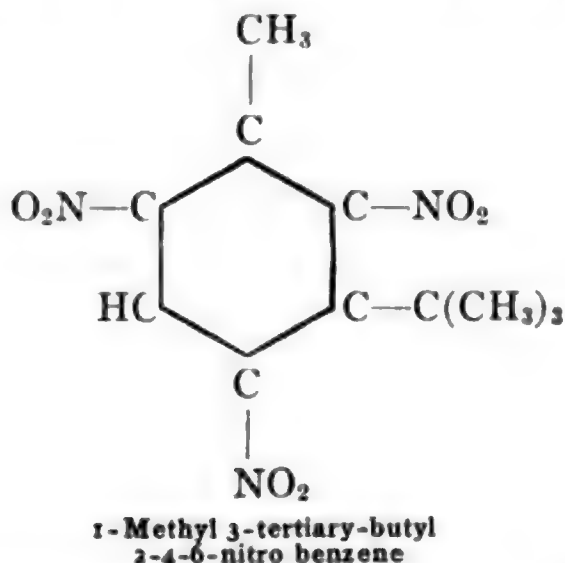
Ammonal is a mixture used for hand grenades and shells. Its composition is ammonium nitrate 58.6 per cent, aluminium powder 21.0 per cent, charcoal 2.4 per cent and T.N.T. 18.0 per cent.

Faversham powder is a mixed explosive permitted and much used in coal mines in England. It is ammonium nitrate 47.5 per cent, potassium nitrate 24 per cent, ammonium chloride 18.5 per cent and T.N.T. 10 per cent.

Nitro Xylenes

Of the three isomeric xylenes, each of which yields nitro products, it is the meta-xylene or 1-3-di-methyl benzene which is most easily nitrated. The number of isomeric nitro xylenes possible has been previously explained (pp. 472 and 482). In the case of meta-xylene three such nitro compounds are possible but only one is readily obtained. It is **1-3-di-methyl 4-nitro benzene**; that is, the nitro group enters the ring ortho to one methyl group and para to the other. This is just what we should expect from the influence of the methyl group upon subsequent substitution (p. 506). The nitro xylenes are not so important as nitro benzene or the nitro toluenes, but have some use in dyestuff manufacture.

One of the higher homologues of benzene yields a very interesting nitro product. When **1-methyl 3-tertiary butyl benzene** is nitrated to a tri-nitro product the three nitro groups enter the 2-4-6 positions.



This compound is known as *artificial musk* as it has an odor very similar to musk, and is used as a substitute for it.

Nitro-alkyl Benzenes.—Isomeric with nitro toluene we have **nitro-methyl benzene**, $\text{C}_6\text{H}_5\text{—CH}_2\text{NO}_2$, which belongs to the group of nitro substitution products in which nitration takes place in the paraffin side-chain and not in the benzene ring. It must be formed, therefore, not by direct nitration, but by reaction between a halogen-alkyl benzene and silver nitrite.



REDUCTION PRODUCTS OF NITRO BENZENE

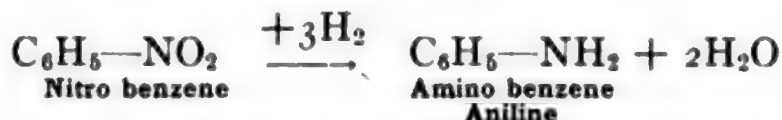
The reactions of nitro substitution products, in which the nitro group is in the ring, are very important, the nitro compounds in general being even more sensitive to reaction than the sulphonic acids. While the latter undergo several different kinds of reactions (p. 519), the nitro compounds yield their most important products by one reaction only, viz., *reduction*. This one type of reaction, under different conditions, yields a very remarkable series of compounds among which are included some of the most valuable dye compounds known. Thus not only in themselves are the nitro products important but also because they are the starting point for other valuable compounds. We may

illustrate these reduction products by means of nitro benzene, bearing in mind that it is typical of any ring nitro compound.

Reduction of Nitric Acid.—When **nitric acid** is reduced by means of hydrogen we obtain as the final reduction product **ammonia**, NH_3 . That is, nitric acid and ammonia stand at the extremes of oxidation and reduction of the element nitrogen.

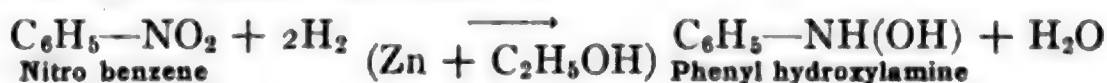


Between nitric acid and ammonia, or between nitric acid and free nitrogen, stand the lower oxidation products of nitrogen, viz., **nitrous** and **hyponitrous acids**, or the **lower oxides of nitrogen**, NO_2 , N_2O_3 , NO and N_2O . In the same way nitric acid substitution products are reduced to ammonia substitution products, *i.e.*, **nitro compounds** are reduced to **amino compounds**.

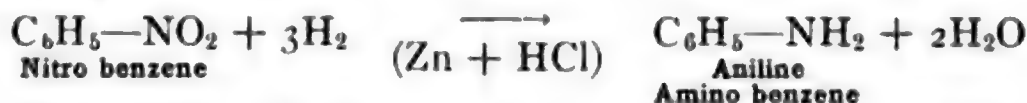


In this reduction of **nitro benzene** to **amino benzene** or **aniline** several intermediate products are formed.

Alcohol and Zinc.—When nitro benzene is reduced in a *neutral* solution, *e.g.*, by means of zinc dust in hot dilute alcohol or in hot water, or by means of aluminium amalgam and water, the nitro benzene loses one atom of oxygen and two atoms of hydrogen are added. The product is known as **phenyl hydroxylamine**.



Acid and Zinc.—When the reduction of nitro benzene takes place in an *acid* solution, *e.g.*, zinc and hydrochloric acid or iron and hydrochloric acid, then the reduction goes to the end and the amino compound, viz., **aniline**, is obtained.



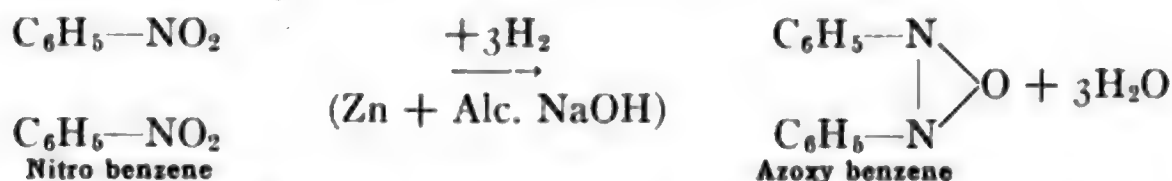
Nitroso-benzene.—Intermediate between nitro benzene and phenyl hydroxyl amine is the nitrous acid derivative or **nitroso benzene**. This compound can not be formed by reduction of the nitro benzene, but is obtained by oxidizing phenyl hydroxylamine.



Expressing the relationship of these three compounds in one series of reactions we have as reduction products of nitro benzene the following:

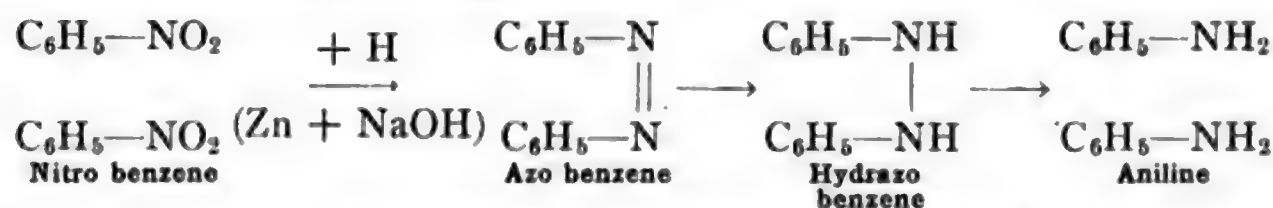


Alcoholic Alkali and Zinc.—A second series of reduction products is formed when the reduction takes place in *alkaline* solution. When nitro benzene is boiled with zinc in an alcoholic solution of an alkali, the reduction affects two molecules of the nitro benzene, which, by the loss of three atoms of oxygen, become united yielding a product known as **azoxy benzene**,

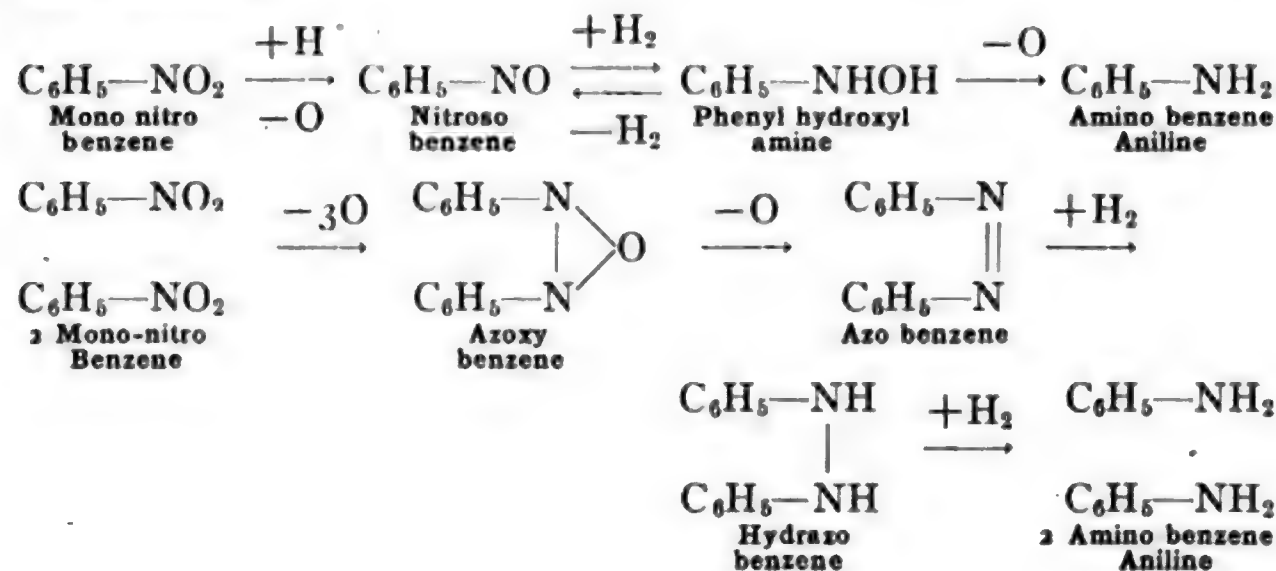


Aqueous Alkali and Zinc.—When the reduction is effected by *stronger alkaline reducing agents*, e.g., zinc and aqueous alkali or by means of sodium amalgam, two molecules of nitro benzene lose all of their oxygen and step by step two and then four atoms of hydrogen are added. The steps in these reductions are as follows:

Azo Benzene, Hydrazo Benzene.—



We have then the following compounds as the reduction products of nitro benzene.



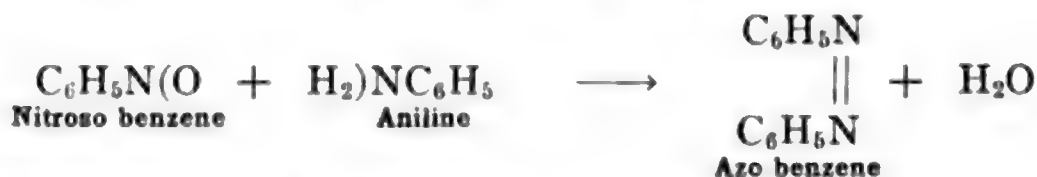
The names *azoxy*, *azo*, *hydrazo* in the above compounds, and also *diazo* which we shall use presently, all come from the French word for nitrogen, *azote*, and signify the presence of nitrogen in characteristic groupings which will be more fully explained later under each compound.

NITROSO COMPOUNDS

Nitroso Benzene.—The *nitroso* or nitrous acid derivatives are exactly analogous to the *nitro* or nitric acid derivatives. As the nitro radical is (NO_2), so the nitroso radical is (NO) and whenever this radical is present, as we found in the nitroso-amines (p. 61), and as we shall find in some more complex compounds of the dye class, it means nitroso derivative. The simplest representative, viz., **nitroso benzene**, $\text{C}_6\text{H}_5\text{—NO}$, differs from nitro benzene in that it is not formed by the direct action of the acid on the hydrocarbon nor, as shown above, is it able to be isolated as a reduction product of nitro benzene. It is prepared, however, by the oxidation of **phenyl hydroxyl amine**, either by means of ferric chloride, FeCl_3 , or of chromic acid, CrO_3 .



The compound is a crystalline solid forming white leaflets, possessing a burning taste. Its melting point is 68° . On melting it is changed to an emerald green liquid which is soluble in ether or ligroin. This change in color and state is perhaps caused by a change from a di-molecular arrangement in the white solid to a mono-molecular arrangement in the green liquid. Nitroso benzene condenses with aniline in acetic acid solution, and is converted into azo benzene.



Nitroso derivatives of the other benzene hydrocarbons need not be considered individually.

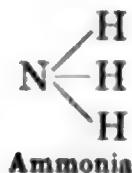
IV. AMMONIA DERIVATIVES OR AMINES

Aniline, $C_6H_5-NH_2$

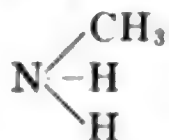
Amino Benzene, Aniline.—The intermediate reduction products obtained from nitro benzene will be considered later and we shall take up now the final product of the reduction, viz., **amino benzene** or **aniline**, and also important derivatives of it.

History.—Aniline has an interesting history and one of especial importance in connection with our present ideas of the constitution of organic compounds. In 1826, **Unverdorben**, while working with **indigo**, obtained by distillation with alcohol a product which formed crystalline salts. He called the compound **crystalline**. In 1834, **Zinnin** obtained a substance from *coal tar* which he called **cyanol**. In 1840, **Fritzsche**, working also on indigo, obtained a substance which he called **aniline** from the Spanish word *anil* for indigo. In 1842, **Runge** reduced nitro benzene with hydrogen sulphide and obtained a compound which he called **benzamine**. Finally in 1843, **Hofmann** worked over these substances and showed that they were all the same compound, the name **aniline** being retained.

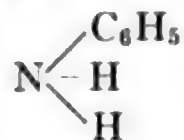
Substituted Ammonia.—Later by a wonderful piece of work, which we have previously referred to in discussing the constitution of the amines (p. 54), Hofmann showed that this aniline and other amines are ammonia compounds resulting from the substitution of organic radicals, either aliphatic or aromatic, in place of one or all of the hydrogen atoms of ammonia. Thus aniline and other substituted ammonias of the benzene series are exactly analogous to the aliphatic amines.



Ammonia

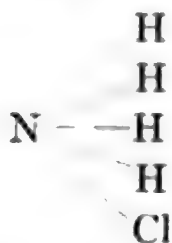


Methylamine

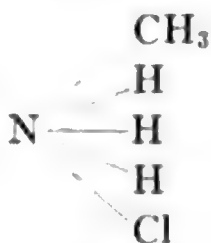


Aniline
Phenylamine

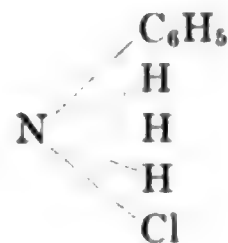
The salts of these compounds are:



Ammonium chloride



Methylamine
hydrochloride
 CH_3-NH_2-HCl



Aniline
hydrochloride
 $C_6H_5-NH_2-HCl$

Preparation of Aniline.—In preparing aniline, nitro benzene is usually reduced by means of tin and hydrochloric acid or iron and hydrochloric acid, the latter being the commercial process. In the reaction with tin, molecular proportions of the tin and acid must be used and the hydrogen produced must be sufficient for the reduction of the nitro benzene. The reaction proceeds as follows:



A secondary reaction then takes place due to the fact that stannous chloride also reduces nitro benzene.



As the aniline forms a salt with hydrochloric acid an extra molecule of acid is required in each of the above reactions. Taking account of this fact and combining the above reactions we may write:

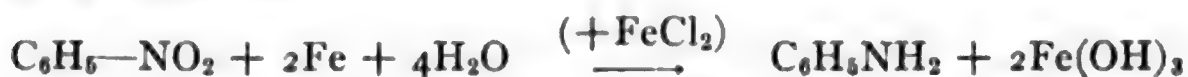


At the end of the reaction the aniline salt is decomposed with alkali, the aniline being set free and it is then distilled with steam. The large amount of stannic chloride present requires a very large amount of excess alkali in order to prevent precipitation of stannic hydroxide. This makes the distillation of the mixture difficult to carry out on an industrial scale.

When the reducing agent is iron and hydrochloric acid an interesting side reaction takes place. Molecular amount of acid is not necessary in this case, only a small amount being required sufficient to start the reaction and form some ferrous chloride. The initial reaction analogous to the one with tin takes place as follows:



In the presence of ferrous chloride, however, metallic iron reacts with water forming **ferric hydroxide** and liberating hydrogen which reduces the nitro benzene. The second stage of the reaction may then be written as follows:



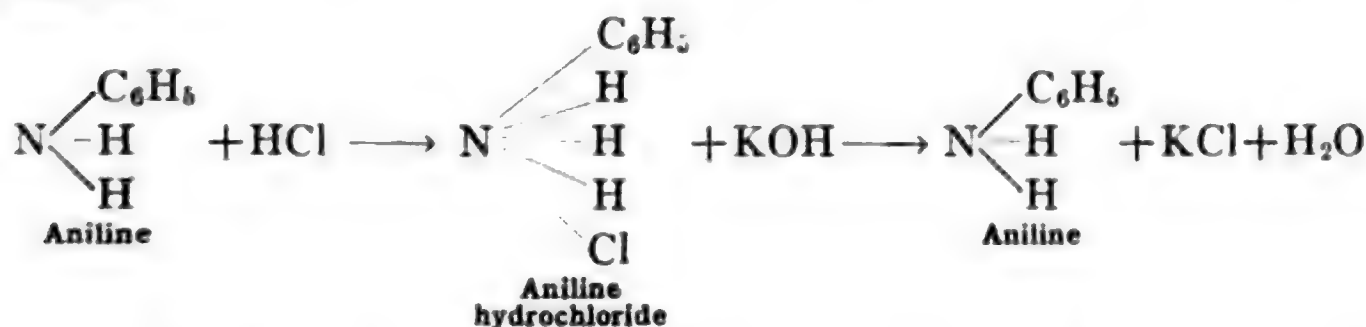
As this requires no acid, only that involved in the initial reaction need

be added. Also as the acid is all used the aniline remains as free aniline and may be distilled with steam without the addition of any alkali. Thus the economy of acid and technical ease of distillation makes this second process the one that is used industrially.

Aniline is a colorless liquid when pure, but it readily oxidizes in the air and becomes dark colored. It melts at -80° and boils at 182.5° , but distils with steam. It is only slightly soluble in water, but is soluble in alcohol and in ether. It is present in coal tar in small amounts and also in bone oil, the product of the distillation of bones.

Aniline Dyes.—Aniline and many of its derivatives, also many related amino derivatives of both benzene and naphthalene hydrocarbons, are of great technical importance in the manufacture of dyes. As the first synthetic dye, **mauve**, was made from aniline the name **aniline dyes** is often used synonymous with **coal tar dyes** for all synthetic dyestuffs, though, as we shall find, there are several groups, some of which are in no sense related to aniline. The dyestuffs and the intermediate products connected with their preparation will be referred to as we come to each compound.

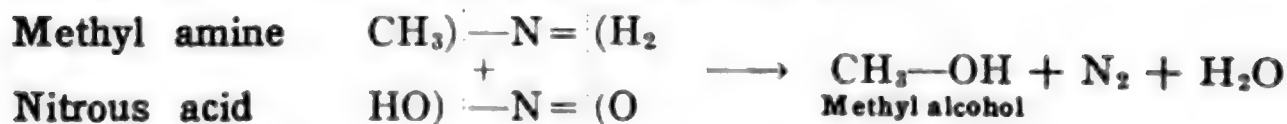
Reactions of Aromatic Amines.—(1) *With acids.* The first prominent reaction of aromatic amines is the one already given, viz., with acids they form salts. These salts are soluble crystalline compounds which, like the ammonium salts, are easily decomposed with strong alkalies yielding the free base. The reactions with aniline are as follows:



(2) *With nitrous acid.* The reaction of the *aromatic primary amines* with nitrous acid is different from that of the *aliphatic primary amines* with the same reagent, and serves to distinguish the two groups of compounds. When a *primary alkyl amine* is treated with nitrous acid the *hydroxyl compound* of the radical is formed and *all of the nitrogen* of the amine is given off as *free nitrogen*. The reaction is as follows:

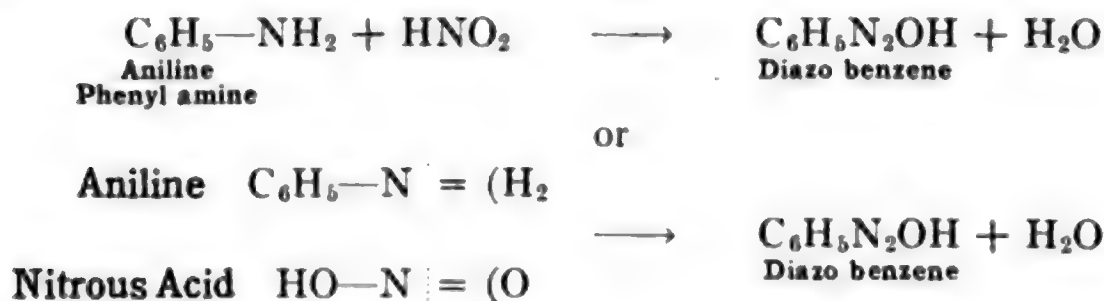


We may represent this very clearly in this way:

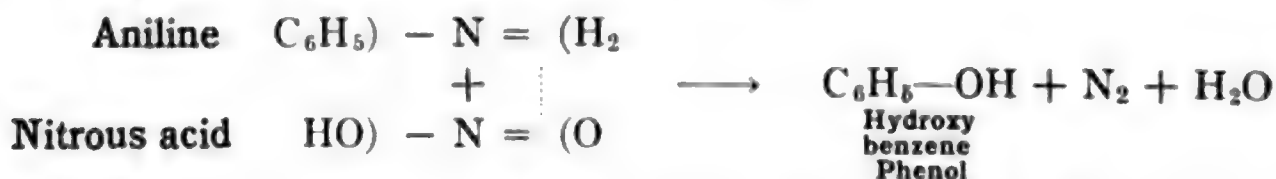


In this reaction there are no intermediate products.

When, however, a *primary aromatic amine* is treated with nitrous acid an intermediate product is formed which belongs to a group of compounds that are both very interesting and important. The reaction with aniline is:



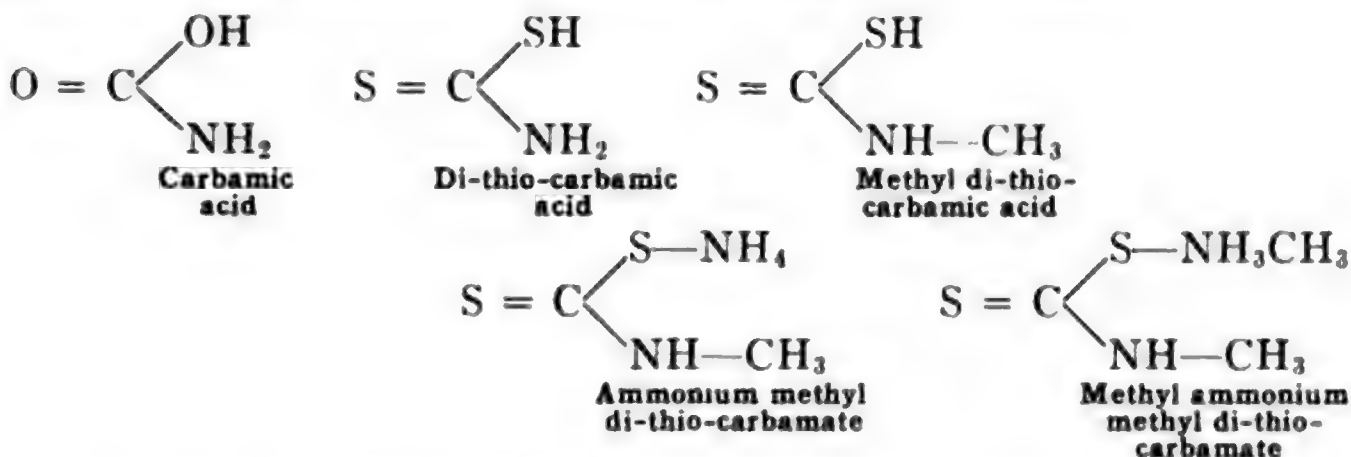
Diazo Benzene.—The products which may be isolated in the form of salts, if the reaction is carried out in the cold, are known as *diazo* compounds, aniline yielding **diazo benzene**. They are strong bases, forming salts which are often extremely explosive when dry, and very unstable toward reagents, undergoing several very important reactions. These will be taken up later. If the reaction is allowed to take place at ordinary or slightly raised temperatures this intermediate diazo compound is not obtained, but the reaction completes itself just as in the case of the aliphatic amines, splitting off all of the nitrogen and forming the hydroxyl compound of the radical.



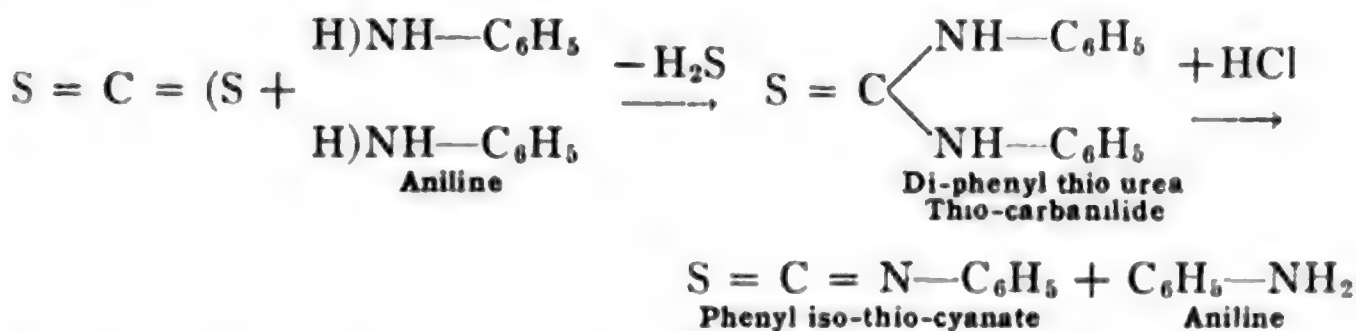
(3) *With carbon disulphide.* Another reaction which distinguishes the aromatic amines from the aliphatic amines is the one with carbon disulphide. When methyl amine is treated with carbon disulphide a product is obtained according to the following reaction:



The product, **methyl ammonium methyl di-thio-carbamate**, is an alkyl ammonium salt, corresponding to the ammonium salt, of methyl di-thio-carbamic acid as shown by the following formulas:



This reaction does not take place with aromatic amines. With aniline, for example, there is obtained instead a compound known as **di-phenyl thio-urea**, hydrogen sulphide being eliminated. On heating the di-phenyl thio-urea with acids one molecule of aniline is lost and phenyl iso-thio-cyanate is obtained (p. 421).

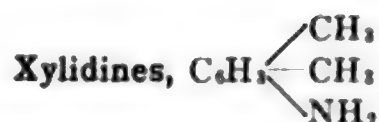


Di-phenyl thio-urea is a di-phenyl derivative of thio-urea, the sulphur analogue of urea.



Anilides.—(4) *With organic acids.* A final reaction to be mentioned with the aromatic amines is that between aniline and carboxyl acids. Just as ammonia forms amides with organic acids so aniline forms compounds known as *anilides*.





Homologous Amines. Toluidines.—The amino derivatives of the homologues of benzene are formed by the same kind of reactions as those for preparing aniline, viz., the reduction of the homologous mono-nitro compounds. The amino toluenes in which the amino group is substituted in the benzene ring are known as **toluidines**, and there are, of course, three isomeric compounds, *ortho*, *meta* and *para*. In the ordinary nitration of toluene the *ortho* and *para* compounds are formed. By indirect methods (p. 532) the **meta-nitro toluene** may also be prepared. These nitro compounds by reduction yield the corresponding toluidines.

These three toluidines have nearly the same properties, e.g., melting point and boiling point, but the aceto derivatives or acet-toluides,



have very different melting points and differ in their solubility. This permits a separation of these isomeric toluidines when it is desired.

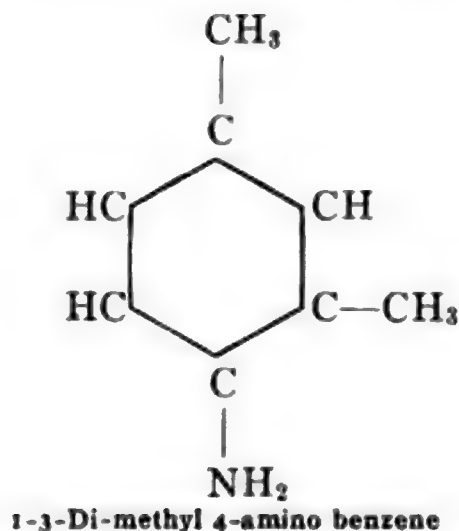
	m.p.	b.p.		m.p.
ortho-Toluidine,	-10.5°C.	218°C.	ortho-Acet-toluide,	110°C.
meta-Toluidine,	+16.0°C.	230°C.	meta-Acet-toluide,	153°C.
para-Toluidine,	+51.0°C.	234°C.	para-Acet-toluide,	63°C.

Dyes.—The toluidines are of great importance in the manufacture of dyes. In making the dye **fuchsine** a mixture of **aniline** and **ortho- and para-toluidine** is used, known as *aniline red*. It is obtained by starting with the distillation product of coal tar known as 50 per cent benzene (p. 498), or the fraction of light oil distillate boiling at 110°–140°. This is nitrated and then reduced. In making the dye **safranine** a mixture of **aniline** and **ortho-toluidine** is used, and this mixture, therefore, is called *aniline for safranine*.

Isomeric with the toluidines are the amino derivatives with the amino group substituted in the side chain, **benzyl amine** or **amino-methyl benzene**, $C_6H_5-CH_2-NH_2$. This reacts in all ways like an alkyl amine.

Xylidines.—The amino derivatives of xylene are known as **xylidines**, and they also are of value for their use in the preparation of dyes. The technical xylene, as used for the preparation of dyestuff xylidines, is a mixture of *ortho*-, *meta*-, and *para*-xylene and the xylidine obtained in

this way is a mixture containing mostly the **unsymmetrical meta-xyli-
dine, i.e.,**



Technical Xylidine.—The **para-xylene** is also present in the technical product which of course yields only one **xylidine**, viz., **1-4-di-methyl 2-amino benzene**. From the *ortho*-xylene present the vicinal or **1-2-di-methyl 3-amino benzene** is obtained. The technical xylidine contains these three isomeric compounds and is used in the preparation of *azo-dyes*. Of the amino derivatives of the higher homologues only one will be mentioned.

Pseudocumidine.—**Pseudocumene** or **1-2-4-tri-methyl benzene** (**unsymmetrical**) yields an amino derivative, viz., **1-2-4-tri-methyl-5-amino benzene**. It is obtained from technical xylidine by simply heating with methyl alcohol.

DERIVATIVES OF AROMATIC AMINES

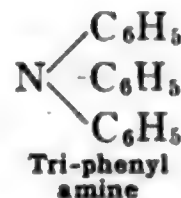
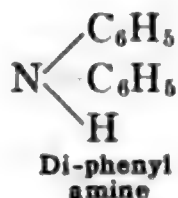
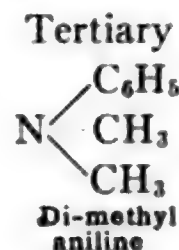
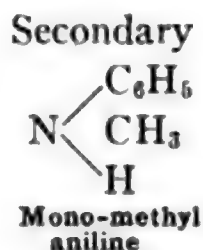
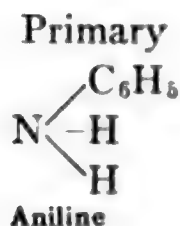
The derivatives of the aromatic amines are of four kinds.

1. *Alkyl or aryl anilines*, etc. Derivatives formed by the introduction of alkyl or aryl radicals into the amino group.
2. *Salts and anilides*, etc. Derivatives formed by the reaction of acids with the amine as an ammonia compound.
3. *Substituted anilines*, etc. Derivatives formed by substitution in the benzene ring.
4. *Anilino acids*. Derivatives formed by substitution of the aromatic amine, as an ammonia compound, into the hydrocarbon radical of an organic acid.

In most cases only the derivatives of aniline will be mentioned, but these may be considered as typical of corresponding derivatives of the other aromatic amines.

1. ALKYL AND ARYL ANILINES

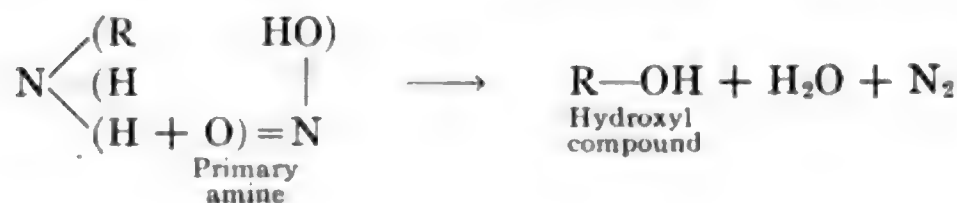
As aniline, toluidine, xyloidine, etc., are *primary amines*, if we substitute alkyl or aryl radicals for one or both of the remaining amino hydrogen atoms we shall obtain secondary and tertiary amines. Such products may be typified by the following in which the *methyl* and *phenyl* radicals are substituted for the amino hydrogen in aniline.

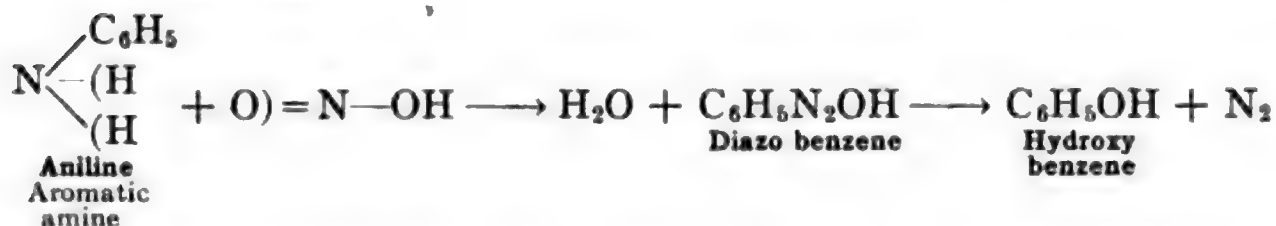


These compounds are exactly analogous to **mono-methyl amine, primary; di-methyl amine, secondary, and tri-methyl amine, tertiary**; and the reactions distinguishing the three groups of aromatic compounds are analogous to those given for the aliphatic amines (p. 59). The resulting products, however, are in some cases distinctly different, showing a difference between the paraffin and benzene compounds.

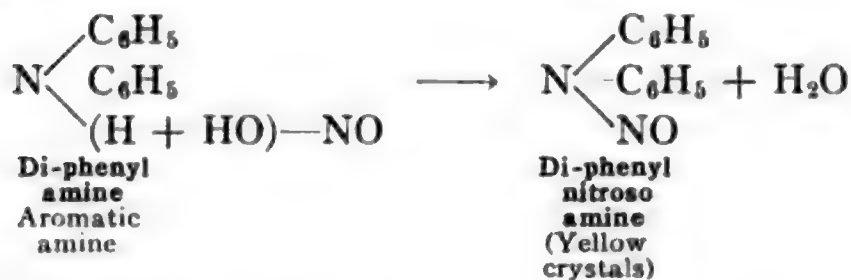
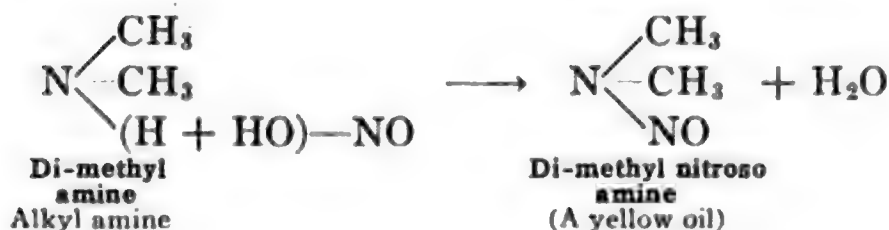
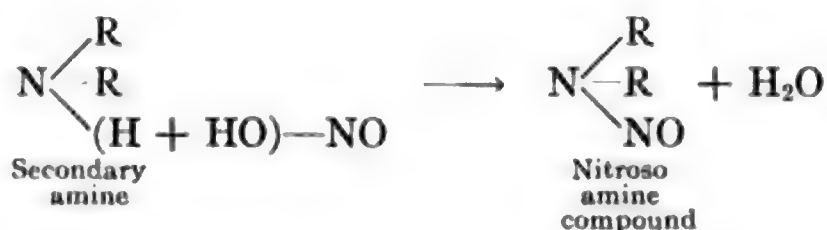
Reactions with Nitrous Acid.—With nitrous acid (HO—NO) primary amines, due to the presence of two remaining ammonia hydrogen atoms, react with the oxygen of nitrous acid which is linked directly to the nitrogen alone. In the case of the alkyl amines the reaction does not stop here, but the hydroxyl group of the nitrous acid unites with the alkyl radical forming an alcohol and the nitrogen is set free.

Primary Amines.—With aromatic amines the reaction may be stopped at the end of the first step and, as recently explained (p. 542), a new type of compound known as a *diazo* compound is obtained. This may be decomposed on raising the temperature and the rest of the reaction effected. This may be illustrated as follows:





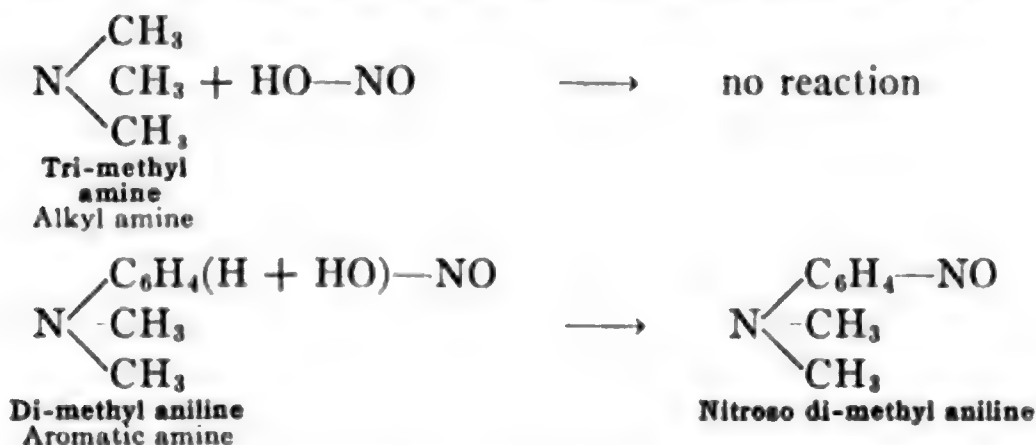
Secondary Amines.—With secondary amines, due to the presence of only *one* remaining ammonia hydrogen atom, the reaction involves only the hydroxyl group of the nitrous acid and the nitroso group, (---NO), enters the amine in place of the remaining ammonia hydrogen. In this case the alkyl amines and the aromatic amines react alike as follows:



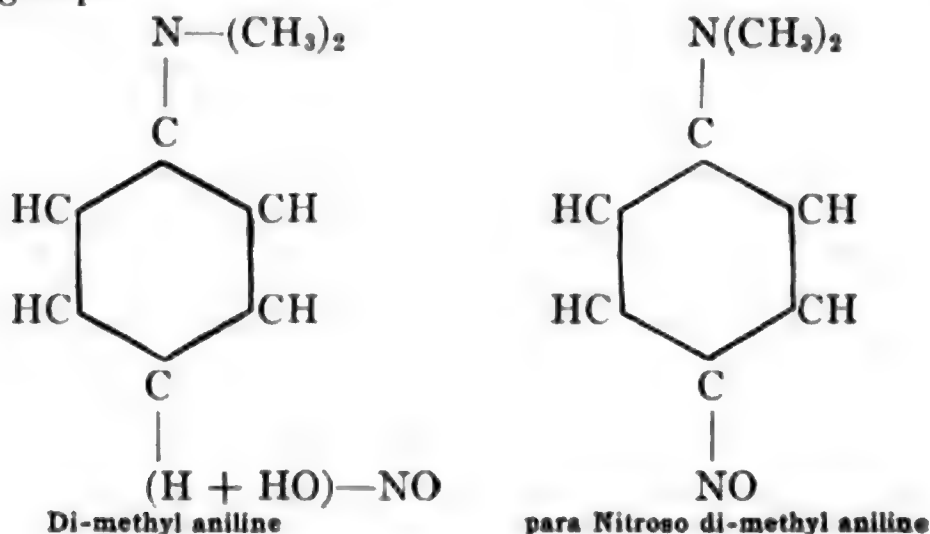
Phenyl Nitroso Amine.—Under certain conditions aniline, a primary aromatic amine, apparently undergoes this same reaction and yields a *nitroso amine*. If the potassium salt of **diazo benzene**, which is obtained from aniline by the action of nitrous acid and which will be explained later (p. 591), is heated, a change takes place involving space relations. The product is isomeric with the diazo compound and is known as the

potassium salt of **iso-diazo benzene**. On acidifying this potassium salt we obtain the free base, **iso-diazo benzene**. This undergoes *rearrangement* and yields $\text{C}_6\text{H}_5\text{—NH(NO)}$ which is **phenyl nitroso amine**. This compound is the same as would be obtained if aniline underwent the nitroso amine reaction characteristic of *secondary* amines, as just described.

Tertiary Amines.—With the tertiary amines, due to the fact that there is *no* remaining ammonia hydrogen atom, no reaction with nitrous acid and the amino group is possible. On this account the *alkyl* tertiary amines undergo no reaction with this reagent. The *aromatic* tertiary amines, however, do react with nitrous acid. As no ammonia hydrogen is present the nitrous acid reacts with a hydrogen of the benzene ring, and the nitroso group is introduced into the ring.



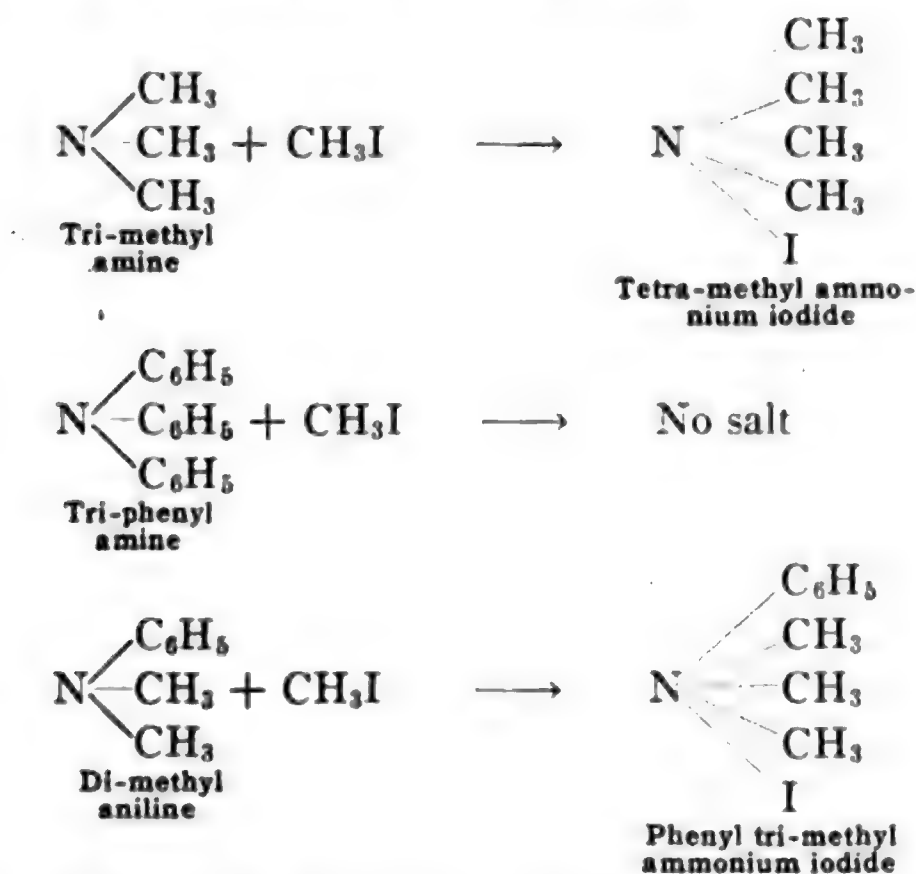
In this reaction the nitroso group enters the ring in the position *para* to the amino group.



These reactions with nitrous acid should be considered in connection with the discussion of the action of nitrous acid on alkyl amines as given in Part I, p. 60.

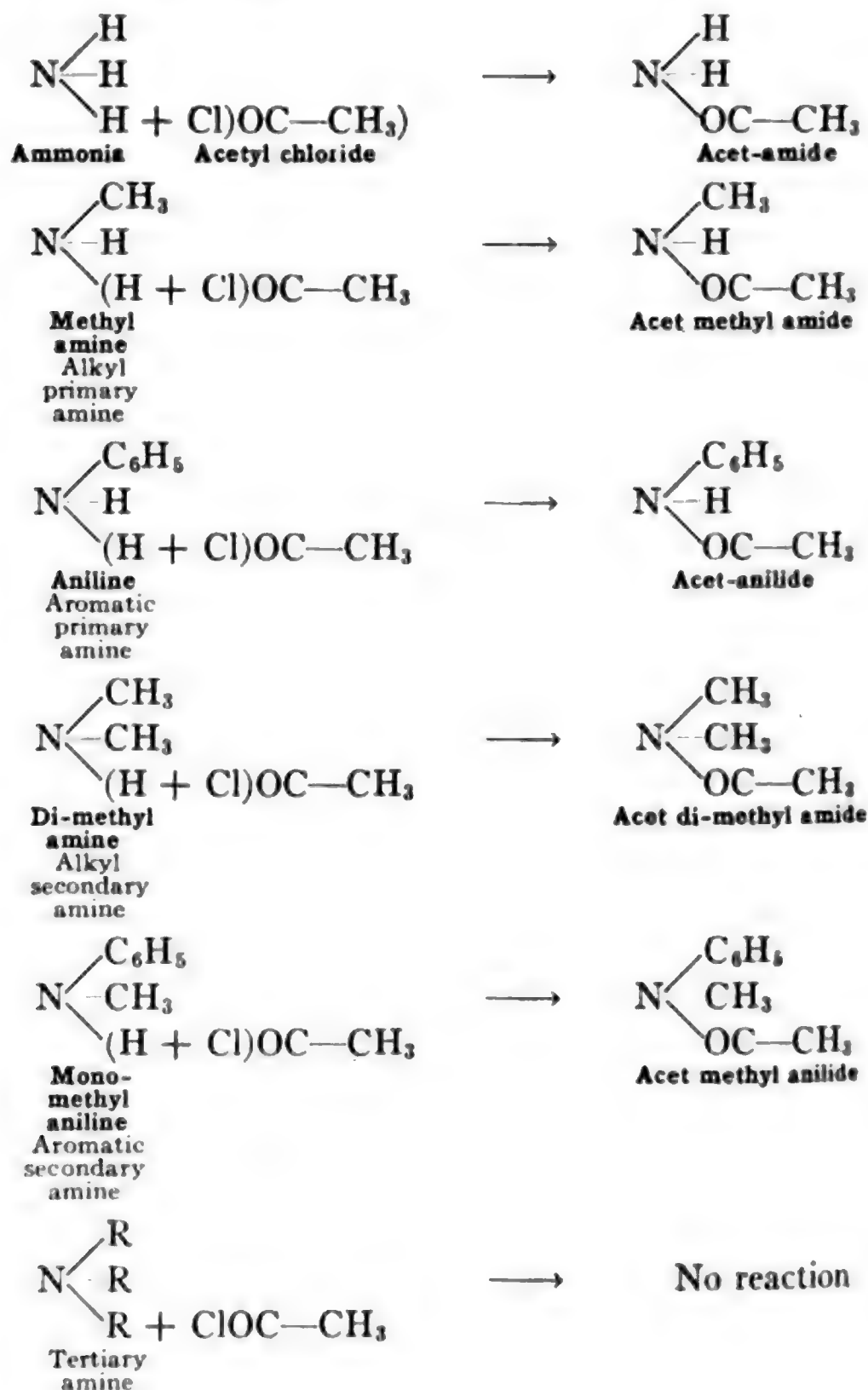
All of the aromatic amines with the exception of tri-phenyl amine, whether primary, secondary or tertiary, are basic and form salts with acids. The basic character of the tertiary aromatic amines varies, however, in degree according to the additional radicals substituted for the amino hydrogen. On this account they react differently toward the alkyl halides.

Reaction with Acids and with Alkyl Halides.—As stated in Part I, the tertiary alkyl amines form salts, with methyl iodide, analogous to ammonium salts. This has been explained as due to the strongly basic character of the tertiary alkyl amines resulting from the substitution of three methyl groups for three ammonia hydrogen atoms. With the tertiary aromatic amines, however, the acid character of the phenyl group neutralizes the basic character of the nitrogen, and in case all of the ammonia hydrogen atoms are substituted by phenyl groups the resulting compound is not basic enough to form salts with alkyl halides or even with acids. If, however, the tertiary aromatic amine contains two methyl groups which are basic in their influence the compound is then basic enough to form salts with alkyl halides.



Reaction with Acetyl Chloride.—With acetyl chloride the amines which contain at least one ammonia hydrogen atom, *i.e.*, primary and secondary, but not tertiary, react just as ammonia itself does with

the same reagent. The reaction takes place with both alkyl amines and with aromatic amines.

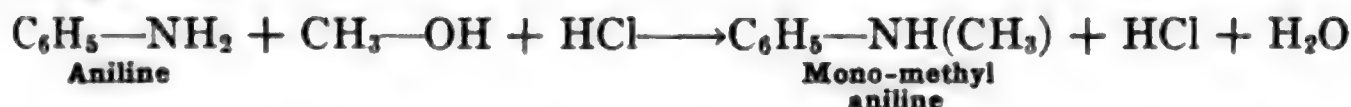


Mono-methyl Aniline, $\text{C}_6\text{H}_5-\text{NH}(\text{CH}_3)$

Di-methyl Aniline, $\text{C}_6\text{H}_5-\text{N}(\text{CH}_3)_2$

The alkyl anilines or alkyl phenyl amines are represented by the above compounds which we have already referred to in the preceding

general discussion of derivatives of aniline. Both are prepared by treating **aniline** with a **methyl halide** or with **methyl alcohol** and a **halogen acid**.



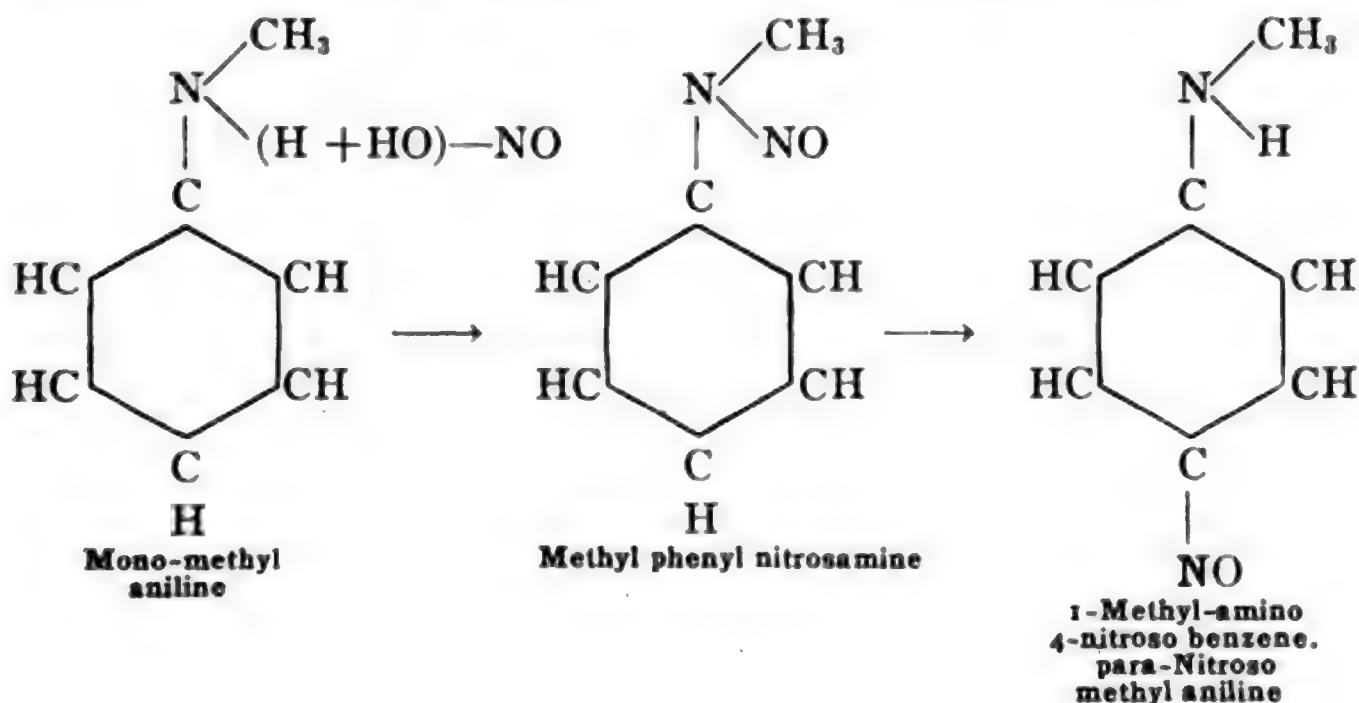
In each of the above reactions the product obtained is the hydrochloride salt of the alkyl aniline.

Mono-methyl aniline, $\text{C}_6\text{H}_5\text{NH(CH}_3\text{)}$, or **methyl phenyl amine**, is a colorless liquid boiling at 193° with a specific gravity of 0.976. In preparing it by the preceding reaction it is always obtained mixed with the di-methyl compound. It may be separated from the latter by con-

version into the non-volatile acyl derivative, viz., $\text{C}_6\text{H}_5\text{—N} \begin{matrix} \text{CH}_3 \\ \text{OC—CH}_3 \end{matrix}$,

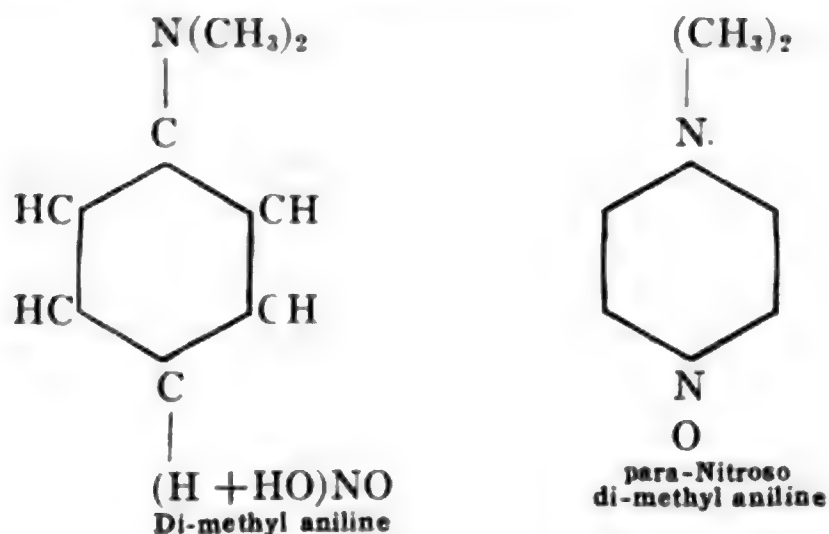
acet methyl anilide. As the di-methyl anilide has no remaining amino hydrogen it forms no acyl derivative, and after treatment of the mixed alkyl anilines with acetyl chloride the di-methyl aniline may be distilled.

Nitrosamine and para Nitroso Methyl Aniline.—The reaction with nitrous acid is characteristic of secondary amines and yields phenyl methyl nitrosamine, the nitroso group entering the amino radical. This, however, undergoes rearrangement with the transference of the nitroso group to the ring yielding a nitroso benzene compound.

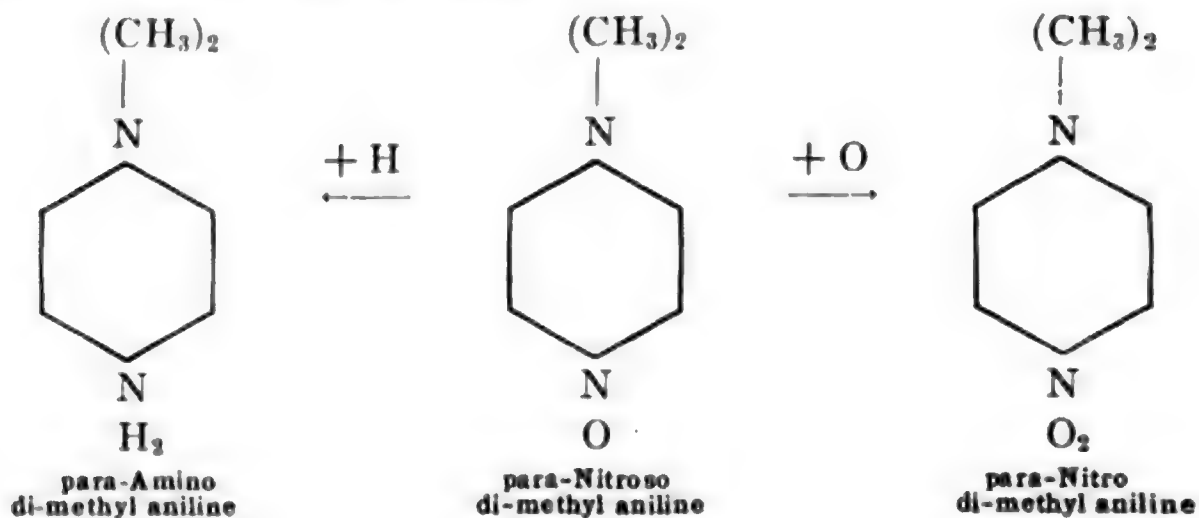


Di-methyl aniline, $C_6H_5-N(CH_3)_2$, is a liquid boiling at the same point as the mono-methyl compound with which it is obtained by the ordinary method of preparation and from which it may be separated by the method just described. It forms well crystallized salts, especially the double salt with **platinum chloride**, viz., $C_6H_5-N(CH_3)_2.HCl.PtCl_4$. This compound crystallizes, with two molecules of water, in ruby colored prisms, which, on loss of water, become reddish-yellow plates. The acid oxalate salt, $C_6H_5-N(CH_3)_2.(COOH)_2$, forms large rectangular plates melting at 139° . With nitrous acid the reaction is the one characteristic of aromatic tertiary amines.

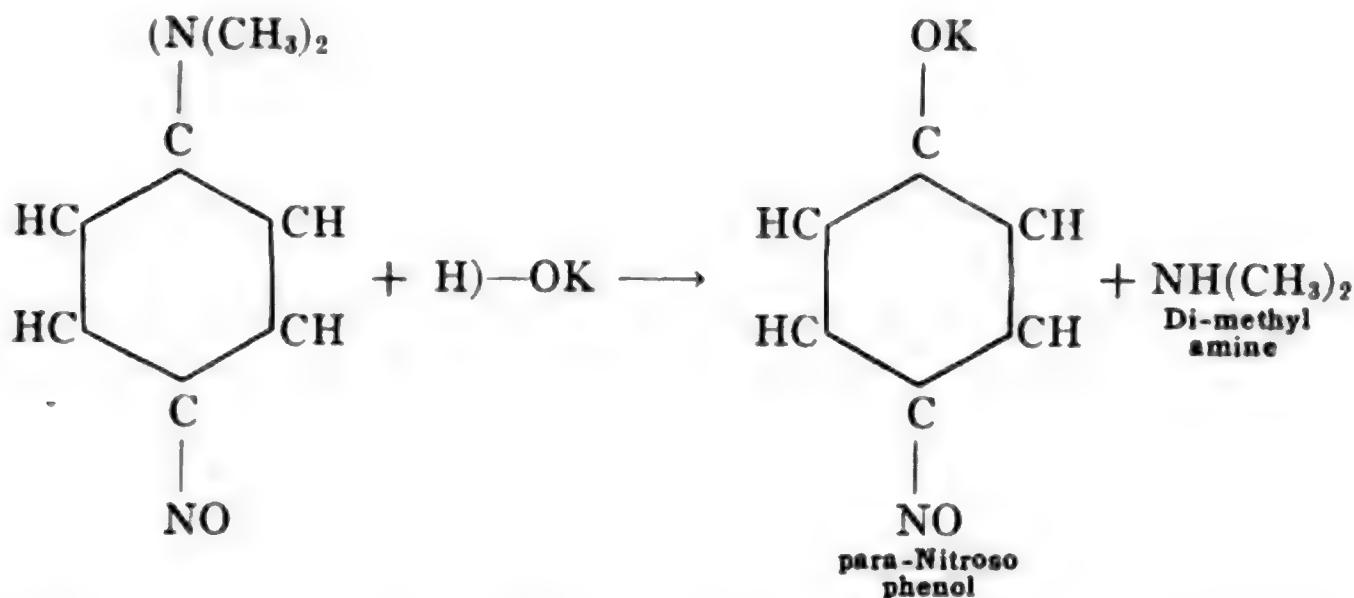
para-Nitroso Di-methyl Aniline.—The (NO) group enters the ring yielding directly a nitroso benzene compound.



This compound crystallizes in beautiful large green leaves, melting point 85° . By *reduction* it goes to **para-amino di-methyl aniline**, and by *oxidation* to para nitro di-methyl aniline.



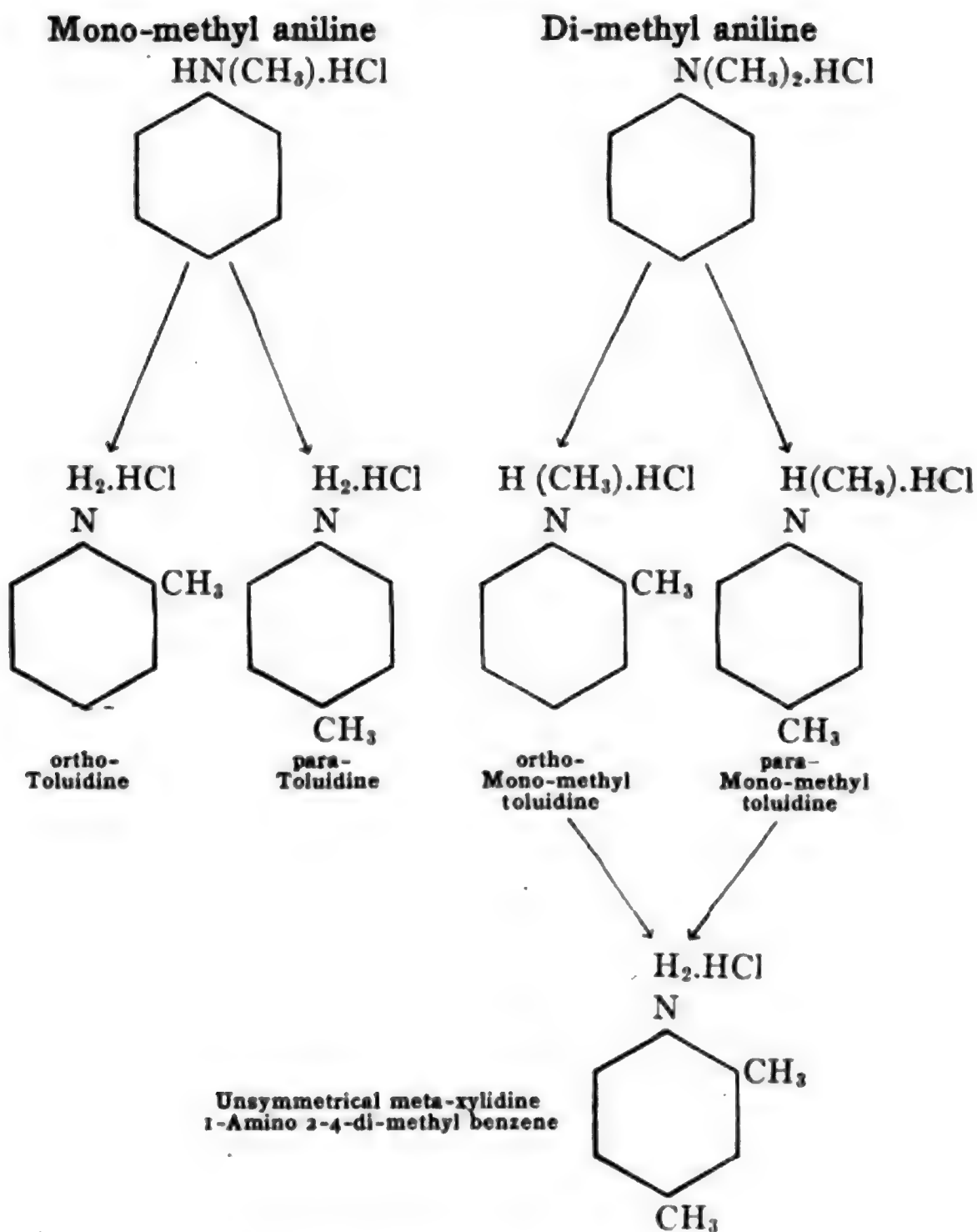
By boiling with KOH it is decomposed into the potassium salt of **nitroso phenol** and **di-methyl amine** and the di-methyl amine thus obtained is pure.



With aniline it forms addition products which separate in beautiful steel blue needles.

Methyl Violet.—A very important reaction of di-methyl aniline is its conversion, by means of mild oxidizing agents, into **methyl violet**. This compound is a **tri-phenyl methane dye** and the reactions involved in its formation will be explained later when we study the dyes of this series.

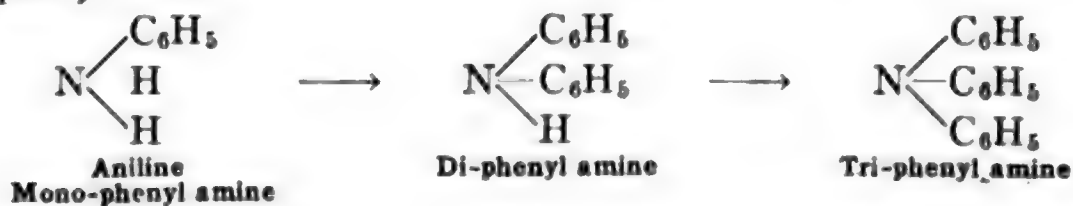
Rearrangement of Alkyl Anilines.—Both mono-methyl aniline and di-methyl aniline undergo an interesting rearrangement when their salts are heated in sealed tubes to 250° – 350° . The **mono-methyl aniline** yields a mixture of **ortho-** and **para-toluidines** while the **di-methyl aniline** yields first a mixture of **ortho-** and **para-mono-methyl toluidines** and then finally from each of these intermediates there is obtained **unsymmetrical meta-xylydine** only. **L. R. WAGENER**



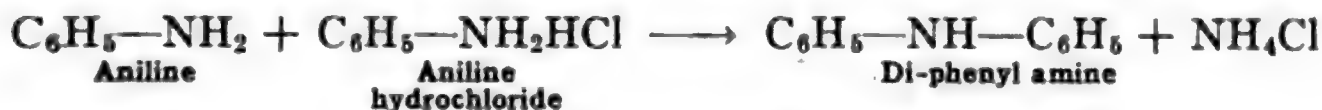
Di-phenyl Amine, $(\text{C}_6\text{H}_5)_2 = \text{NH}$

Tri-phenyl Amine, $(\text{C}_6\text{H}_5)_3 = \text{N}$

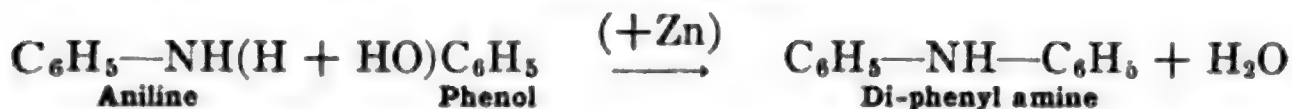
Corresponding to the alkyl anilines we have the phenyl anilines or *poly-phenyl amines*.



Di-phenyl amine was discovered by Hofmann in 1864. It is basic in character but weaker than aniline. It is prepared by heating together **aniline hydrochloride** and **aniline** to 240° .



It may be prepared also from **phenol**, **aniline** and **zinc**.

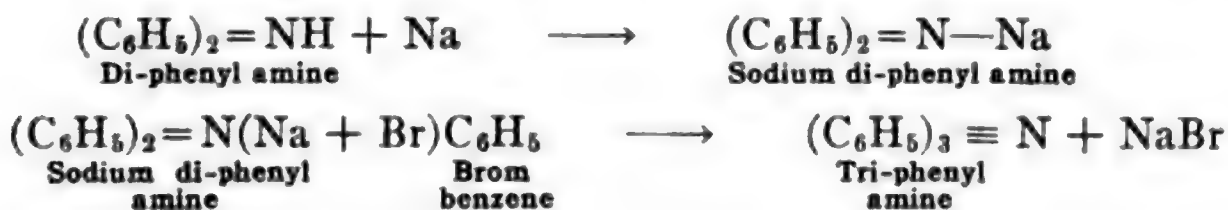


This latter is an important reaction for preparing the homologues. *R* represents *phenyl*, *tolyl*, *xylyl*, etc.



Di-phenyl amine crystallizes from ligroin in white leaflets with faint odor; melting point 54° , boiling point 302° . It is soluble in alcohol, ether and benzene and slightly soluble in water. A solution of di-phenyl amine in sulphuric acid, *i.e.*, di-phenyl amine sulphate, is colored blue by a trace of nitric acid, and is used as a test for nitrates. In the color industry di-phenyl amine makes *azo dyes*.

Tri-phenyl amine is prepared by treating a boiling solution of sodium in di-phenyl amine with **brom benzene**. The acid influence of the phenyl radicals gives to di-phenyl amine the property of forming a sodium compound which then reacts with the brom benzene.



It crystallizes from ether in large pyramidal crystals; melting point 127° . It is soluble in hot alcohol, and a little in cold alcohol. It has lost *all* of the *basic* properties of the ammonia and does *not* form salts with acids. This shows the negative or acid influence of the phenyl radical as compared with the methyl radical.

2. SALTS AND ANILIDES, ETC.

The salts of aniline and its homologues are the simplest derivatives which the aromatic amines form with acids.



These compounds need no further explanation as they were fully discussed under the reactions of aniline. The hydrochloride, acetate, sulphate and nitrate are all common substances. They are all soluble crystalline bodies. The reactions of the aromatic amines with nitrous acid have been discussed.

Acetanilide, $C_6H_5-NH-OC-CH_3$,

With organic acids aniline forms not only the salts just discussed but also derivatives analogous to the amides. When aniline is treated with acetic acid at ordinary temperature the simple salt is first obtained.



When this is boiled for some time water is lost and **acetanilide** is obtained.



This reaction is analogous to the formation of acetamide from ammonium acetate by the loss of water (p. 145).



The anilide is better prepared by the ordinary method of introducing the acetyl group, viz., by using **acetyl chloride** or **acetic anhydride**.

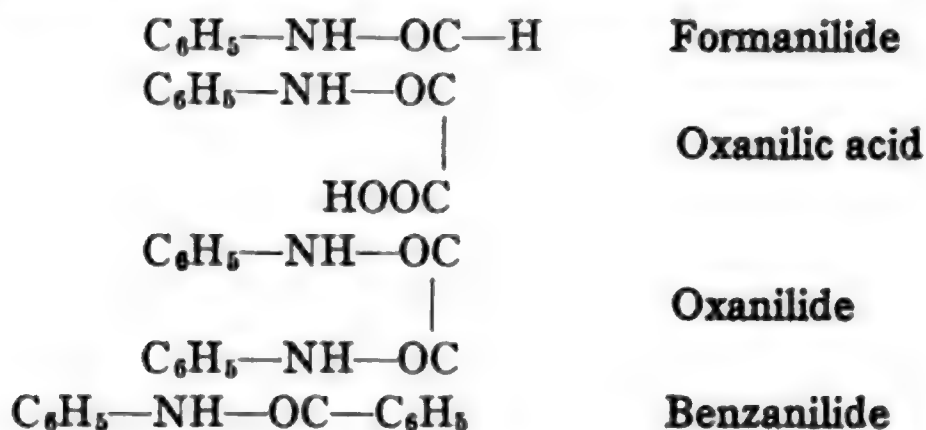


This reaction is also analogous to the one between ammonia and acetyl chloride by which acetamide is formed.

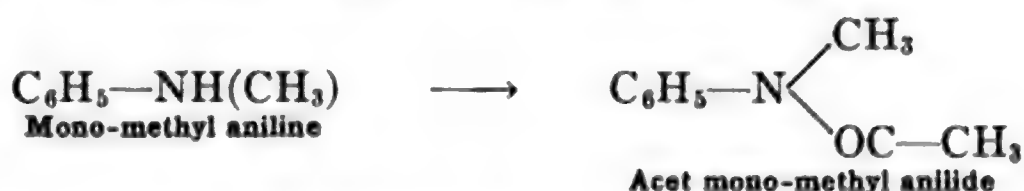


Antifebrin.—Acetanilide is a common medicinal substance much used as a fever reducer under the name of antifebrin. It is a solid, crystallizing in glistening plates; melting point 112° . It is slightly soluble in cold water, readily in hot water. Though not an ester it easily hydrolyzes reforming aniline and acetic acid. Other known anilides formed from aniline and formic acid, oxalic acid and benzoic

acid, etc., are known. Oxalic acid forms two derivatives, one acid and one neutral, analogous to **oxamic acid** and **oxamide** (p. 272).



Di-anilides.—Aniline also yields *di-anilides* in which both amino hydrogen atoms are replaced by acid groups, *e.g.*, **di-acetanilide**, $\text{C}_6\text{H}_5\text{—N}=(\text{OC—CH}_3)_2$. Anilides are also formed from the alkyl anilines of the *secondary* group but not of the *tertiary*.



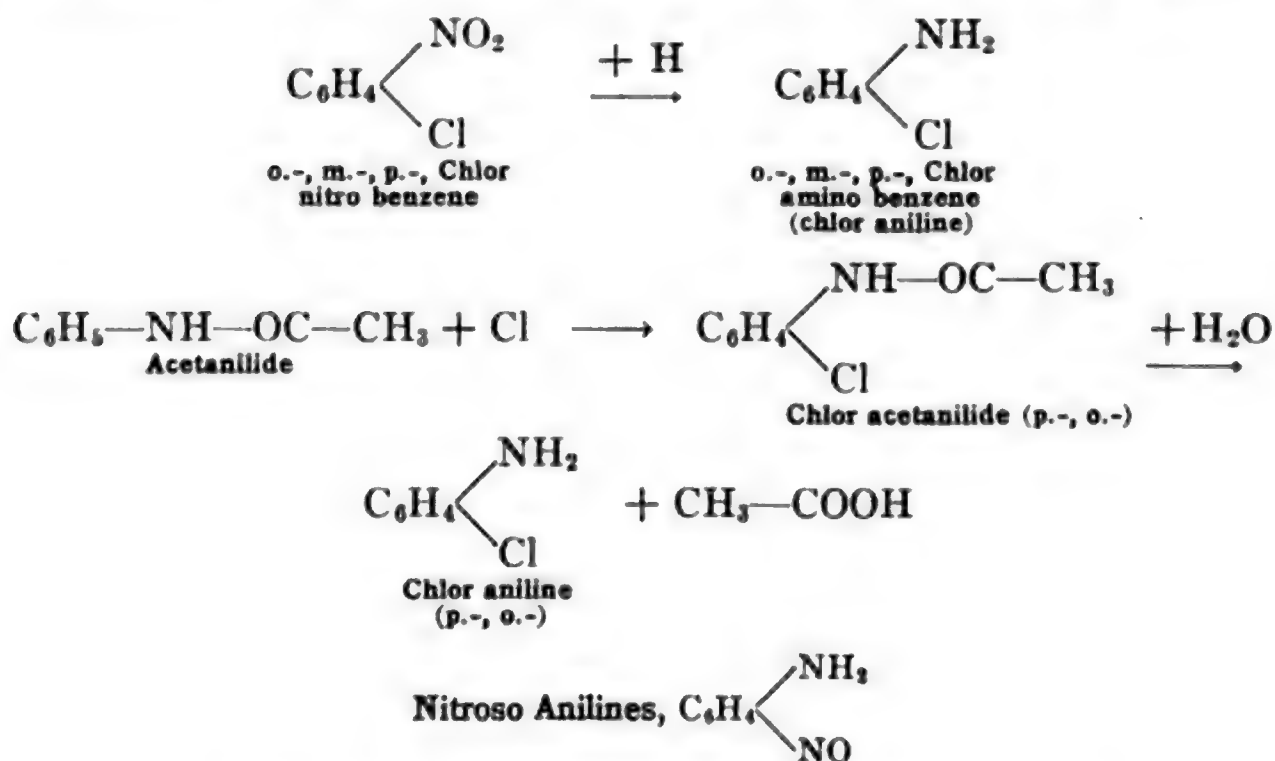
Toluidides have been referred to (p. 544). The xylidides and other homologues need not be considered individually.

3. SUBSTITUTED ANILINES, ETC.

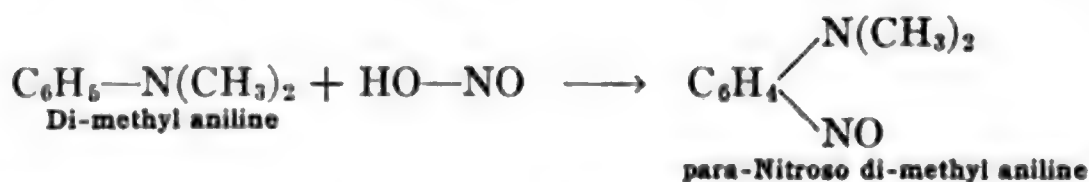
The derivatives of aromatic amines resulting from substitution in the ring are of two classes: (a) Substitution of hydrocarbon radicals. (b) Substitution of non-hydrocarbon groups, *e.g.*, *halogens*, *nitro*, *nitroso*, *sulphonic acid*, *hydroxyl*, *carboxyl groups*, etc. The first class is of course identical with the homologues of aniline which we have already considered. In the second class the compounds containing the hydroxyl group or the carboxyl group substituted in the ring will be considered under the hydroxyl and carboxyl derivatives of benzene, *i.e.*, the *phenols* and *acids*. This leaves for present treatment those compounds formed by substituting in the ring of aniline or its homologues a *halogen*, *nitroso*, *nitro* or *sulphonic acid* group.



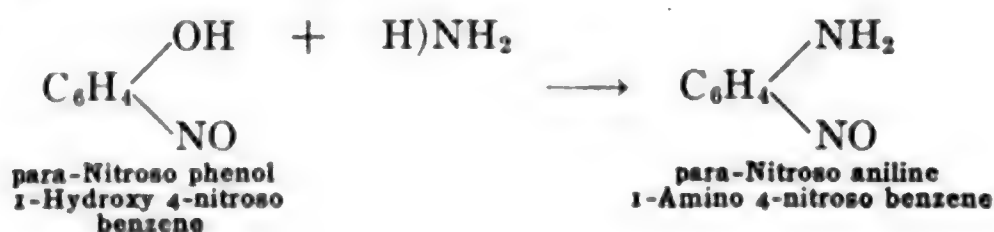
The direct chlorination or bromination of aniline takes place more easily than that of benzene, the result being the **symmetrical tri-chlor** or **tri-brom aniline**, viz., **1-amino 2-4-6-tri-chlor benzene**, $C_6H_2Cl_3(NH_2)$; and **1-amino 2-4-6-tri-brom benzene**, $C_6H_2Br_3(NH_2)$. The **mono-halogen anilines** are prepared by reducing **mono-chlor nitro benzenes**, or by halogenating acetanilide and then hydrolyzing.



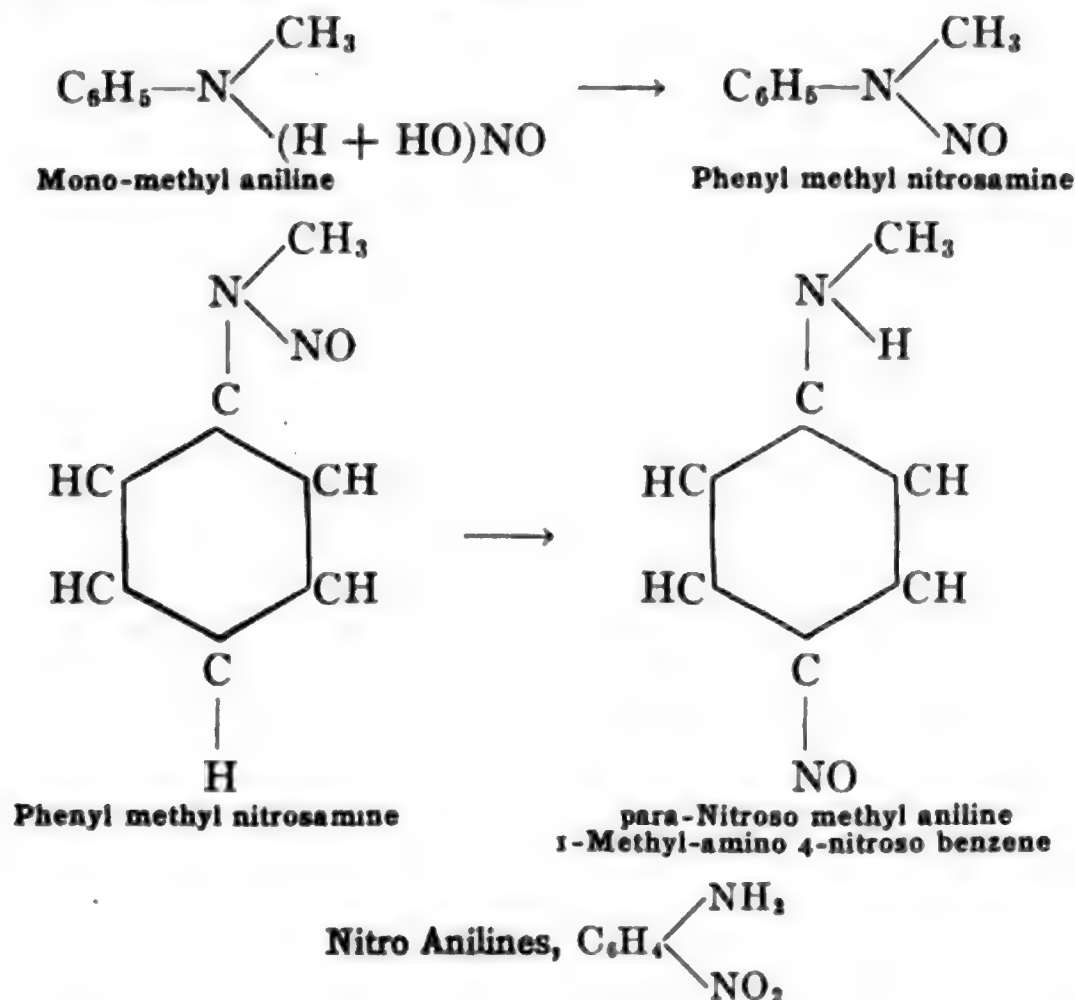
Nitrous acid derivatives in which the nitroso group enters the ring are formed by the direct action of nitrous acid only in the case of the tertiary amines, *e.g.*, **di-methyl aniline** as already described (p. 552).



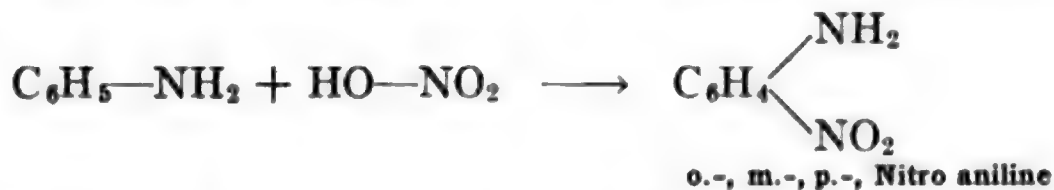
In the case of aniline itself this direct action with nitrous acid does not occur as previously explained. By starting with **nitroso phenol**, however, the amino group may be introduced in place of the hydroxyl by direct action of ammonia.



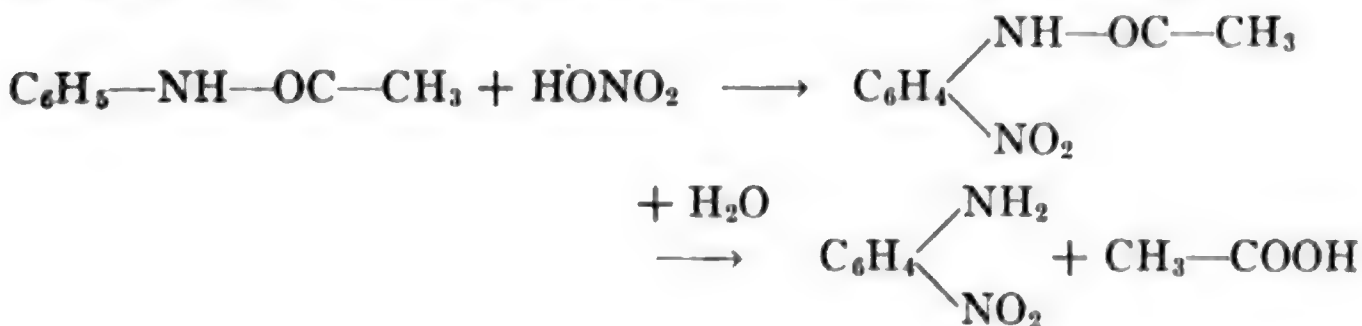
The nitroso substitution products of secondary amines, *e.g.*, **mono-methyl aniline**, $\text{C}_6\text{H}_5\text{—NH}(\text{CH}_3)$, are formed by a rearrangement of the nitrosamine which itself is formed by the direct action of nitrous acid on the secondary amine (p. 547).



The nitration of amino benzene (aniline) takes place readily, the nitro group entering the ring mostly in the *ortho* and *meta* positions.



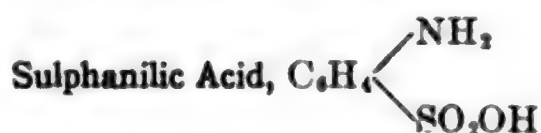
Nitration also takes place directly with the anilides (acetanilide or benzanilide), which may then be hydrolyzed yielding nitro aniline. In this case the *para* compound is obtained almost exclusively,



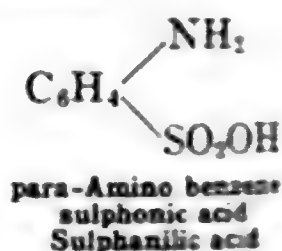
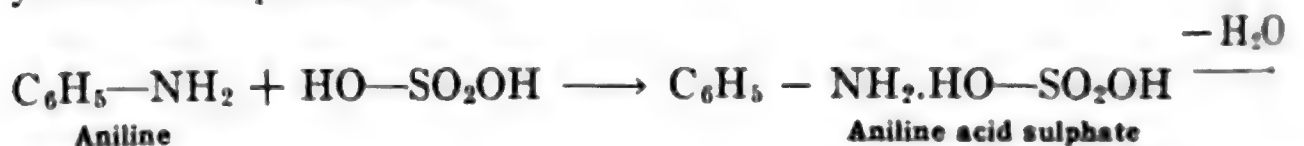
These nitro anilines known as nitranilines, especially the *para* and *meta* compounds, are used in the dyestuff industry in making *azo dyes*.

Di-methyl aniline also forms a known nitro product, but mono-methyl aniline does not. Di-nitro products analogous to the mono-nitro products are known in some cases.

Sulphonic Acid Derivatives



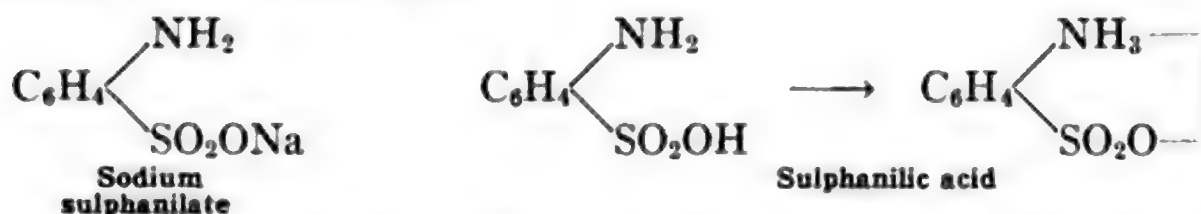
As in the case of halogenation and nitration the sulphonation of aniline takes place more easily than that of benzene itself. When aniline is heated with concentrated or fuming sulphuric acid the sulphonic acid group enters the ring in the *para* position. The first reaction of the sulphuric acid on the aniline is of course the formation of the salt, **aniline acid sulphate**, but this loses water on heating and yields the sulphonic acid.



This compound is known as sulphanilic acid. It may also be considered as an amino derivative of benzene sulphonic acid, i.e., **para-amino benzene sulphonic acid**. Its name, **sulphanilic acid**, is in agreement with its relation to aniline and sulphuric acid. It is distinctly different from sulphonic acids of the hydrocarbons in being difficultly soluble in cold water. As we shall see later, it is of great importance in the preparation of dyes. It is a crystalline compound soluble in alkalies as the alkali salt, but is precipitated as the free acid on acidifying the solution of the salt.

Inner Salt Constitution.—The fact that the alkali salts of sulphanilic acid readily react with acetic anhydride resulting in the introduction of the acetyl radical into the amino group, while the free acid does not

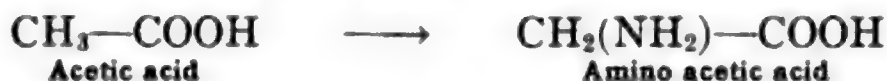
so react, supports the view that the free acid is an inner salt in which there is no free amino group.



The sulphonic acids of the aniline homologues and derivatives are all crystalline compounds. Di-sulphonic acids of the aromatic amines are also known.

4. ANILINO ACIDS

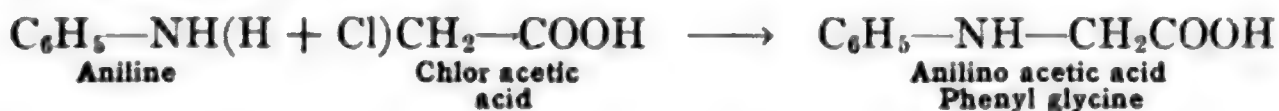
When ammonia is substituted in organic acids in place of a hydrogen atom of the hydrocarbon radical we obtain *amino acids*.



Aniline acting as ammonia forms derivatives analogous to these called *anilino acids*.

Anilino Acetic Acid, $\text{CH}_2(\text{C}_6\text{H}_5\text{—NH})\text{—COOH}$ Phenyl Glycine

Analogous to amino acetic acid we have **anilino acetic acid**, better known as **phenyl glycine**, which is formed by the action of aniline upon **chlor acetic acid**.



As this is plainly a phenyl derivative of glycine or amino acetic acid it is known as **phenyl glycine**. Similar derivatives of other aliphatic acids are known.

POLY-AMINO BENZENES

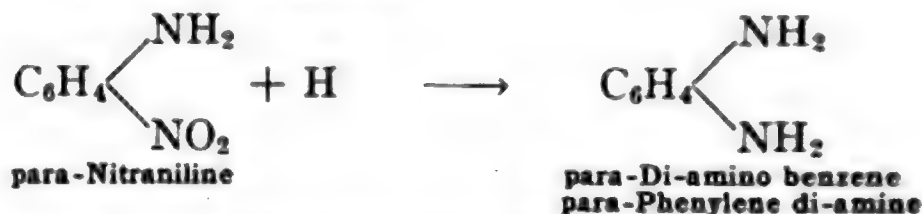
One group of ammonia derivatives of the benzene hydrocarbons has still to be considered, viz., that in which more than one amino group is substituted in the hydrocarbon.



When **di-nitro benzene** is reduced we obtain **di-amino benzene**.



As the di-nitro benzene ordinarily prepared is the *meta* compound the di-amine obtained from it is also *meta*. If, however, instead of reducing **di-nitro benzene** we start with the partially reduced product, viz., **nitraniline** (p. 559), which is prepared largely as the *para* compound, we then obtain the **para-di-amine**.



The ortho di-amino benzene prepared by the reduction of **ortho-nitraniline** is of special interest because of certain condensation reactions which it undergoes with **aldehydes**, **ketones** and **nitrous acid**. The *meta* compound also shows a characteristic reaction with nitrous acid. The *para* compound is readily oxidized and gives characteristic color reactions with ferric chloride and hydrogen sulphide. It is of importance in the preparation of dyes. All of these di-amines are colorless, crystalline solids which can be distilled.

They differ from the mono-amines in being easily soluble in water. They form salts with acids reacting with two equivalents because of the two amino groups.



Di-amino derivatives of the secondary amines, **mono-methyl aniline**, and the tertiary amines, **di-methyl aniline**, are also known. Of these compounds the **para-amino di-methyl aniline** is the most important in the dyestuff industry. *Tri-amino*, *tetra-amino*, *penta-amino* and *hexa-amino* derivatives of benzene and also **penta-amino toluene** are all known.

Relation to Dyes.—The amino derivatives of benzene and its homologues, which we have been discussing (pp. 539, etc.), form an especially important group of compounds in connection with the manufacture of synthetic dyes. Some of the compounds are themselves dyes while others are intermediate products in the preparation of dyes. When we consider all of the various forms in which the amino group may be present and the different relations which it may have to the benzene ring we can not fail to realize the vast possibilities in the preparation of dyes and the industrial importance of these amino compounds.

V. NITROGEN COMPOUNDS INTERMEDIATE BETWEEN NITRO BENZENE AND ANILINE

Among the nitrogen compounds of benzene we have also those intermediate compounds formed in the reduction of nitro benzene to aniline (p. 535). These are as follows:

Nitroso benzene,	$\text{C}_6\text{H}_5\text{—NO}$
Phenyl hydroxyl amine,	$\text{C}_6\text{H}_5\text{—NH—OH}$
Azoxy benzene,	$\begin{array}{c} \text{C}_6\text{H}_5\text{—N} \\ \\ \text{C}_6\text{H}_5\text{—N} \end{array} \begin{array}{c} \diagup \\ \diagdown \end{array} \text{O}$
Azobenzene,	$\begin{array}{c} \text{C}_6\text{H}_5\text{—N} \\ \\ \text{C}_6\text{H}_5\text{—N} \end{array}$
Hydrazo benzene,	$\begin{array}{c} \text{C}_6\text{H}_5\text{—NH} \\ \\ \text{C}_6\text{H}_5\text{—NH} \end{array}$

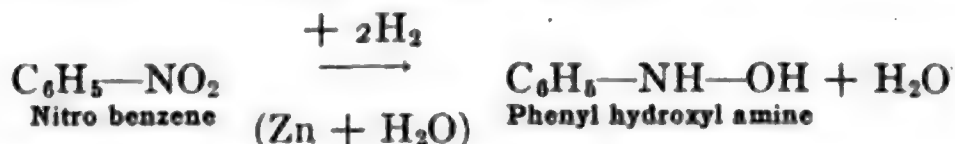
Also related to these and best considered at this time we have:

Phenyl hydrazine,	$\text{C}_6\text{H}_5\text{—NH—NH}_2$
Di-azo benzene,	$\text{C}_6\text{H}_5\text{—N=N—OH}$

The first of these compounds, nitroso benzene, has been fully considered as the nitrous acid derivative of benzene (p. 538).

Phenyl Hydroxyl Amine, $\text{C}_6\text{H}_5\text{—NH—OH}$

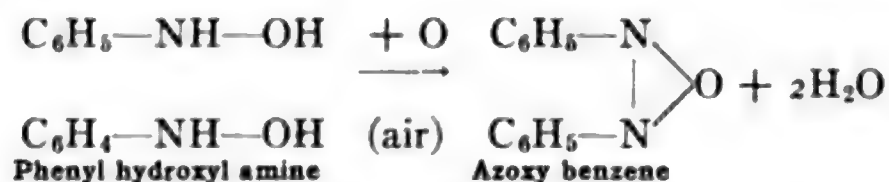
When nitro benzene is reduced in neutral solutions by means of *zinc in hot water* or hot alcohol or when an ether solution of it is reduced by means of *aluminium amalgam and water*, or when it is reduced *electrolytically*, the product is **phenyl hydroxyl amine**.



Phenyl hydroxyl amine is the phenyl derivative of **hydroxyl amine**, $\text{NH}_2\text{—OH}$, which was considered in Part I (p. 63). Like the parent

substance, phenyl hydroxyl amine is a base and forms salts with acids, *e.g.*, $\text{C}_6\text{H}_5\text{—NH—OH.HCl}$, **phenyl hydroxyl amine hydrochloride**. It is a solid crystallizing in silky needles which melt at 81° . It is slightly soluble in cold water and quite easily in hot water, alcohol, ether and hot benzene. It is easily oxidized and reduces **Fehling's solution**.

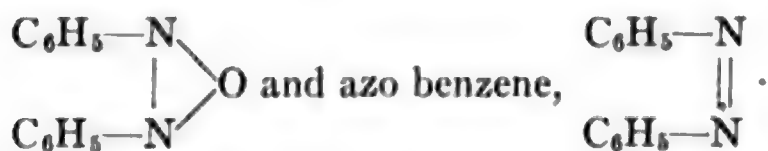
Oxidation Products.—With different oxidizing agents it yields various products. Its water solution oxidizes easily in the air and yields **azoxy benzene**.



With stronger oxidizing agents, *e.g.*, **chromic acid**, CrO_3 , or **ferric chloride**, FeCl_3 , it yields **nitroso benzene**.

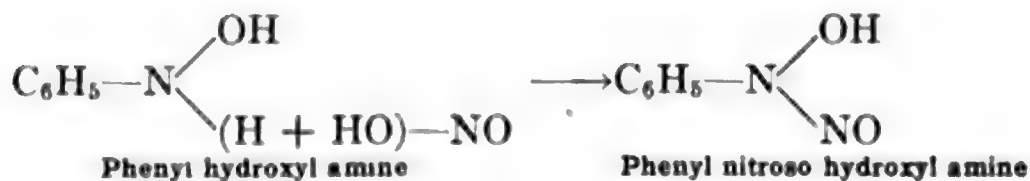


When boiled with water it is partly volatilized, but is mostly converted into a mixture of nitroso benzene, $\text{C}_6\text{H}_5\text{—NO}$; azoxy benzene,

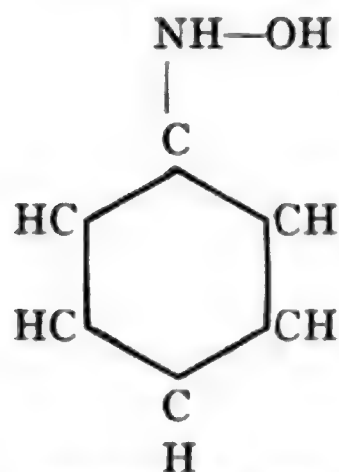


It is very sensitive to the action of alkalies and by them is converted first into **nitro benzene**, $\text{C}_6\text{H}_5\text{—NO}_2$, and then into **azoxy benzene**.

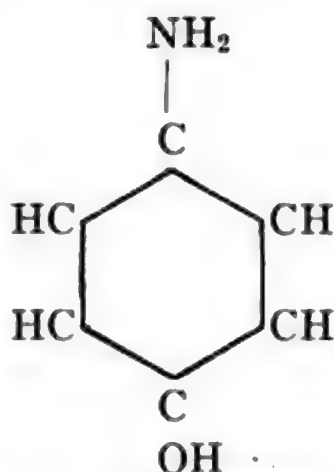
Phenyl Nitroso Hydroxyl Amine.—Phenyl hydroxyl amine is a *secondary* amine, one hydrogen of ammonia being replaced by the *phenyl* group and another by the *hydroxyl* group. With nitrous acid, therefore, it acts as secondary amines do, yielding a **nitroso amine**



Molecular Rearrangement to para-Amino Phenol.—Phenyl hydroxyl amine undergoes an important molecular rearrangement. When boiled with mineral acids it is converted into **para-amino phenol**.

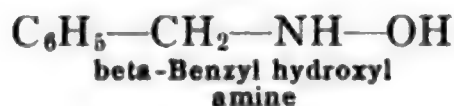
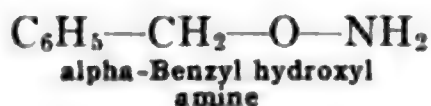


Phenyl hydroxyl amine

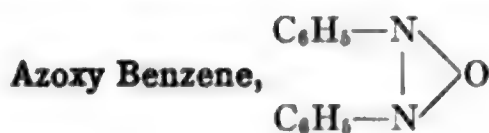
para-Aminophenol
1-Amino 4-hydroxy benzene

The rearrangement occurs also when **nitro benzene** is electrolytically reduced by immersing the cathode in nitro benzene and sulphuric acid and the anode in sulphuric acid. Phenyl hydroxyl amine is first produced and by the above rearrangement is converted into **para amino phenol**. This rearrangement is analogous to the one occurring when **phenyl methyl nitrosamine** goes over to **para-nitroso methyl aniline** (p. 559).

Benzyl Hydroxyl Amine.—One of the hydroxyl amines of the benzene homologues is of importance in illustrating a case of isomerism. The compound is the hydroxyl amine derivative of toluene with the hydroxyl amine group substituted in the side chain, *i.e.*, it is **benzyl hydroxyl amine**. The isomerism is due to the different hydrogen atoms of the hydroxyl amine which the benzyl group replaces. The two compounds are;

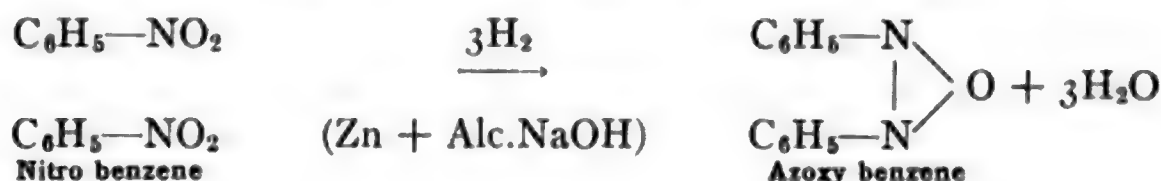


In the **alpha** compound the benzyl group replaces the *hydroxyl hydrogen* of hydroxyl amine while in the **beta** compound it replaces one of the *amino hydrogens*. There are also known two isomeric **di-benzyl hydroxyl amines** and one **tri-benzyl hydroxyl amine**.



Azoxy benzene is the product of the reduction of two molecules of nitro benzene by means of *alcoholic sodium hydroxide and zinc*. The

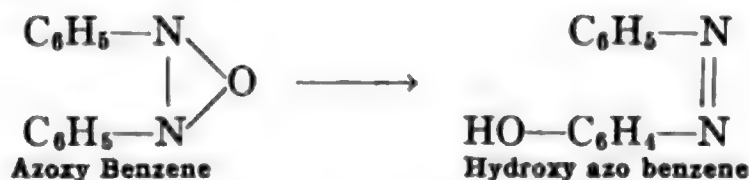
reaction results in the loss of three atoms of oxygen from two molecules of nitro benzene and the union of the two molecules into one.



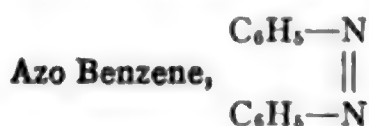
As has just been stated, it is also formed by the oxidation of phenyl hydroxyl amine even in the air. In this case there is a loss of four hydrogens and one oxygen from two molecules.



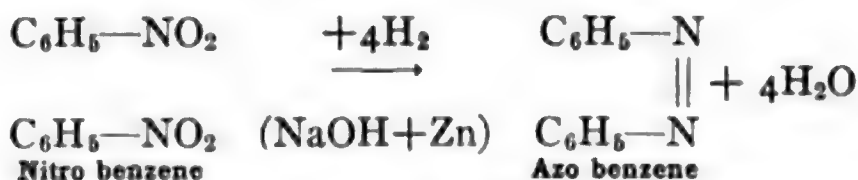
Azoxy benzene is a crystalline compound melting at 36° , soluble in alcohol and in ether. On reduction it passes to the other intermediate products closer to aniline, viz., **azo benzene** and **hydrazo benzene** and finally to **aniline** itself.



Rearrangement.—Like nitroso methyl aniline and phenyl hydroxyl amine it undergoes molecular rearrangement as above.

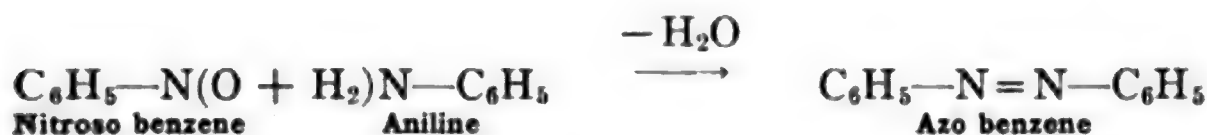


Nitro benzene when subjected to more energetic reduction by means of *aqueous sodium hydroxide and zinc* loses all four oxygen atoms from two molecules and the two nitrogens become linked together by a double bond, the product being known as **azo benzene**.

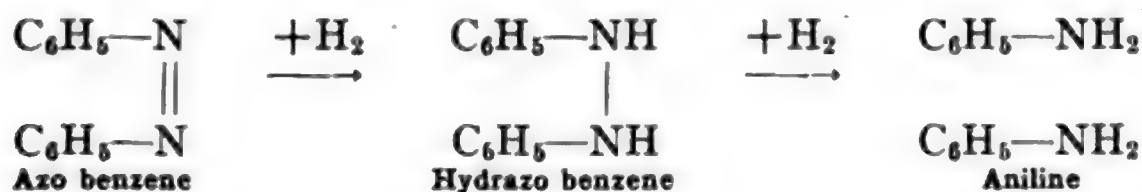


It is also formed by the further reduction of azoxy benzene or by the oxidation of hydrazo benzene.

From Nitroso Benzene and Aniline.—The most interesting method of preparing **azo benzene** is by the *condensation* of **nitroso benzene** and **aniline**.



This reaction shows clearly the relationship between these three compounds. By reduction azo benzene yields **hydrazo benzene** and then **aniline**. In this reduction the doubly linked nitrogen group is broken by the addition first of one hydrogen atom to each nitrogen and then by the addition of one more hydrogen atom to each nitrogen with the splitting of the double molecule into two molecules of aniline.



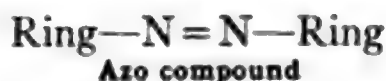
Azo benzene is a solid forming glistening orange-colored crystals. It melts at 68° and boils at 295°.

Homologous Azo Compounds.—**Azo toluenes** and **azo xylenes**, of which there are isomeric forms, are known as well as azo compounds of other substituted benzenes. Azo benzene is not usually prepared by the reactions given above but by other reactions to be described under *derivatives of azo compounds* in which group most of the important azo compounds will be found. By these reactions azo compounds are formed in which the azo nitrogen group links two rings which may be alike, as in **azo benzene** or **azo toluene**, giving us *symmetrical* compounds, or the two rings may be unlike, either unsubstituted or substituted, giving us *unsymmetrical* compounds. Formulas for a few examples may be given.

Azo benzene	$\text{C}_6\text{H}_5\text{—N=N—C}_6\text{H}_5$	<i>Symmetrical</i>
Azo toluene	$\text{H}_3\text{C—C}_6\text{H}_4\text{—N=N—C}_6\text{H}_4\text{—CH}_3$	<i>Symmetrical</i>
Benzene azo toluene	$\text{C}_6\text{H}_5\text{—N=N—C}_6\text{H}_4\text{—CH}_3$	<i>Unsymmetrical</i>
Amino azo benzene	$\text{C}_6\text{H}_5\text{—N=N—C}_6\text{H}_4\text{—NH}_2$	<i>Unsymmetrical</i>
Di-methyl amino azo benzene	$\text{C}_6\text{H}_5\text{—N=N—C}_6\text{H}_4\text{—N(CH}_3\text{)}_2$	<i>Unsymmetrical</i>

Other azo compounds of the benzene homologues or other hydrocarbons, or of aniline and its derivatives, need not be considered. They will either be discussed in the next section under derivatives of azo compounds or if not discussed individually they will be mentioned in connection with important products made from them.

Azo Compounds.—The term **azo** is derived from the French word for nitrogen, viz., *azote*. Compounds designated by the name **azo** or some modification of it, e.g., **azo benzene**, **oxy azo benzene**, **amino azo benzene**, **hydrazo benzene**, **azoxy benzene**, etc.; represent a class of compounds in which *two nitrogen atoms, each of which is linked to a separate benzene ring, are directly linked to each other by a double or single bond*.



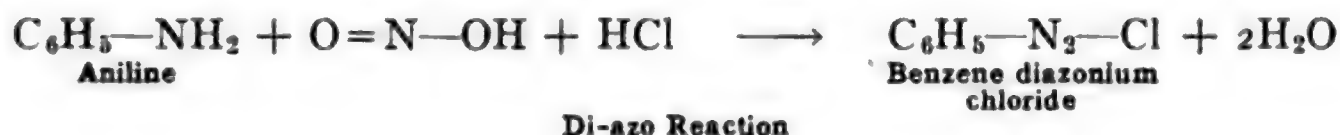
In the true *azo* compounds, the first three mentioned above, the nitrogen atoms are *doubly linked* to each other, while in the *hydrazo* and *azoxy* compounds the double bond is broken by the addition of a hydrogen atom to each nitrogen or the second bond of each nitrogen is linked to a connecting oxygen atom (see formulas preceding). In these compounds the benzene rings may be either benzene itself or one of its homologues, or they may be one of the more complex ring compounds to be studied later. The rings may have various substituting groups in them and these groups may also contain nitrogen. Also the two rings may be alike or different, yielding symmetrical and unsymmetrical azo compounds. Whatever the modification may be, however, the grouping above is characteristic of all true *azo compounds*.

Di-azo Compounds.—Contrasted with the *azo compounds* we have another group known as the *di-azo compounds*. As the name indicates these also contain *two nitrogen atoms* and these nitrogens are also directly linked to each other, but *only one nitrogen atom is linked to a benzene ring*.



The full discussion of these diazo compounds with the explanation of their constitution will come later; but, as they are involved in the preparation of some of the azo compounds, it is necessary to introduce the subject at this time. They are formed by the action of nitrous acid

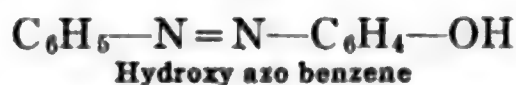
on the primary aromatic amines. We thus speak of *diazotizing an amine* or we term the reaction *diazotization*.



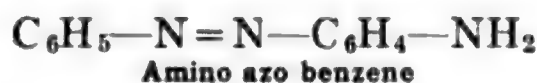
DERIVATIVES OF AZO COMPOUNDS

AMINO AZO COMPOUNDS

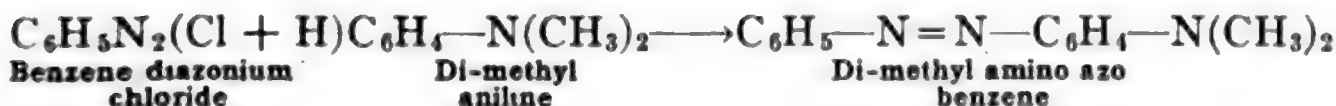
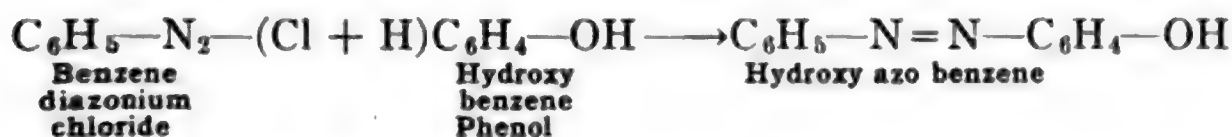
Two important classes of derivatives of the azo compounds which include some very valuable dyes are the *amino azo* and *hydroxy azo* compounds. The latter which are also called oxy azo compounds are derivatives of the azo compounds resulting from the substitution of one or more hydroxyl groups in the rings.



The *amino azo* compounds are exactly analogous, having one or more amino groups in the rings.



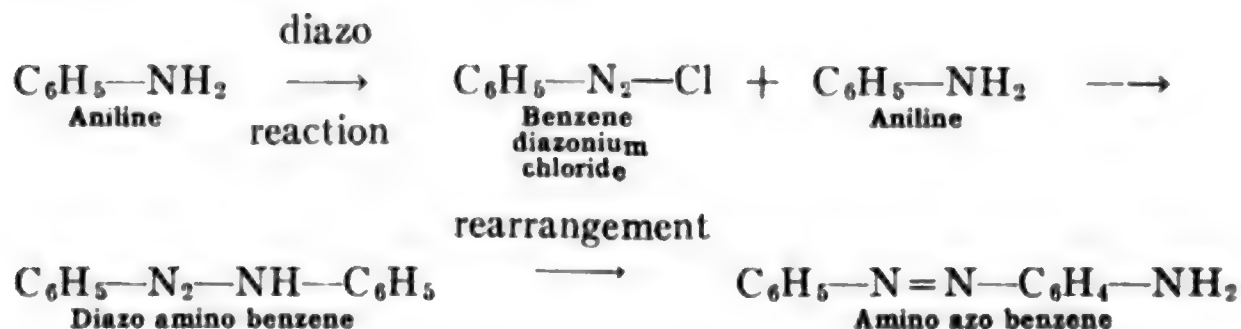
Griess Diazo Reaction.—The most important method for preparing both of these classes of compounds is that of **Griess**, by means of the *diazo compounds* (p. 589). He found that when a salt of a diazo compound reacts with a *hydroxy benzene* compound or with an *amino benzene* compound, especially one containing a *tertiary* amine group, *e.g.*, **di-methyl aniline**, the following reactions take place by which the ring of the *diazo* compound is coupled, by means of the two nitrogens, with the ring of the second compound thus forming an *azo* compound.



He found that *tertiary* amines like di-methyl aniline react easily, but that *primary* amines react in this way only when there are two such

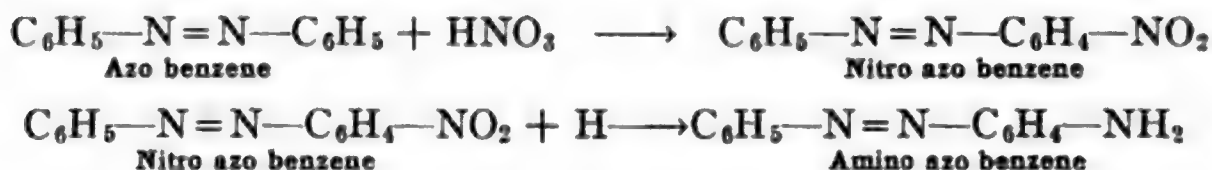
primary amine groups present and in the *meta* position to each other, the reaction taking place in weakly acid solution.

Diazo amino Compounds.—In the case of *para* primary di-amines and primary mono-amines such as **aniline**, the reaction does not take place in this way. It was found later, however, that primary mono-amines did yield azo compounds by a molecular rearrangement of an intermediate *diazo amino compound*.

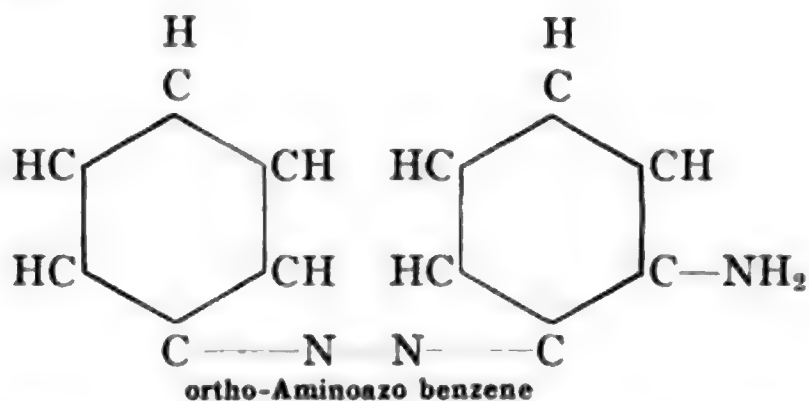
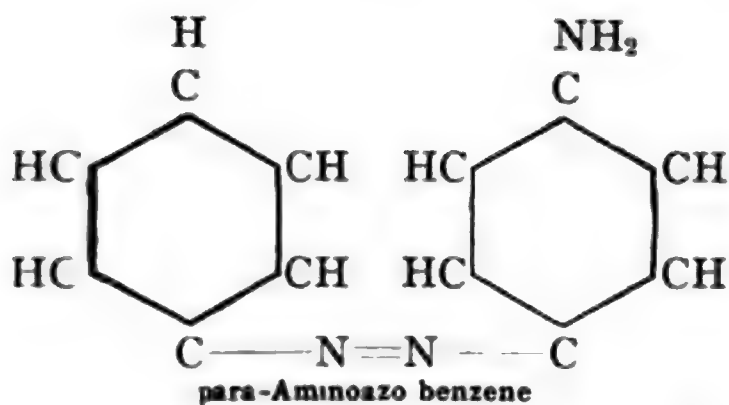


Thus by means of the **Griess reaction** it is possible to start with an amino compound, diazotise it and then couple up the diazo compound with an undiazotized amino compound and obtain the amino azo compound either directly or after molecular rearrangement.

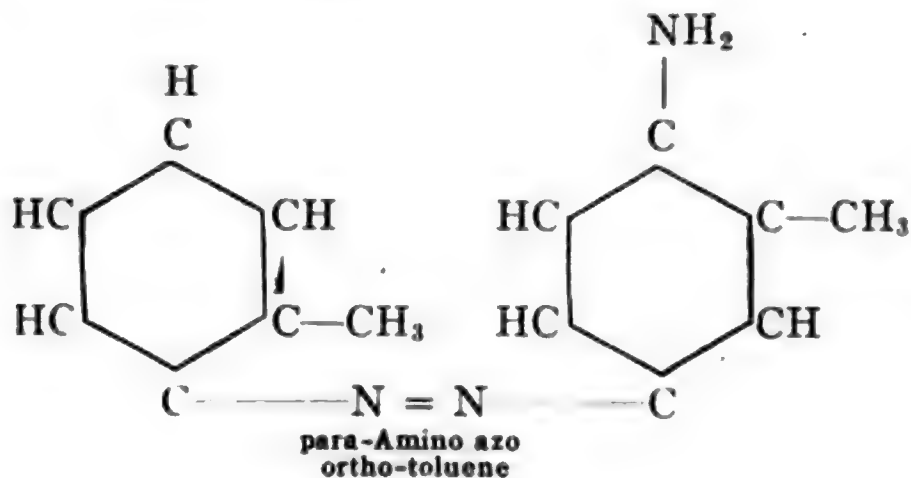
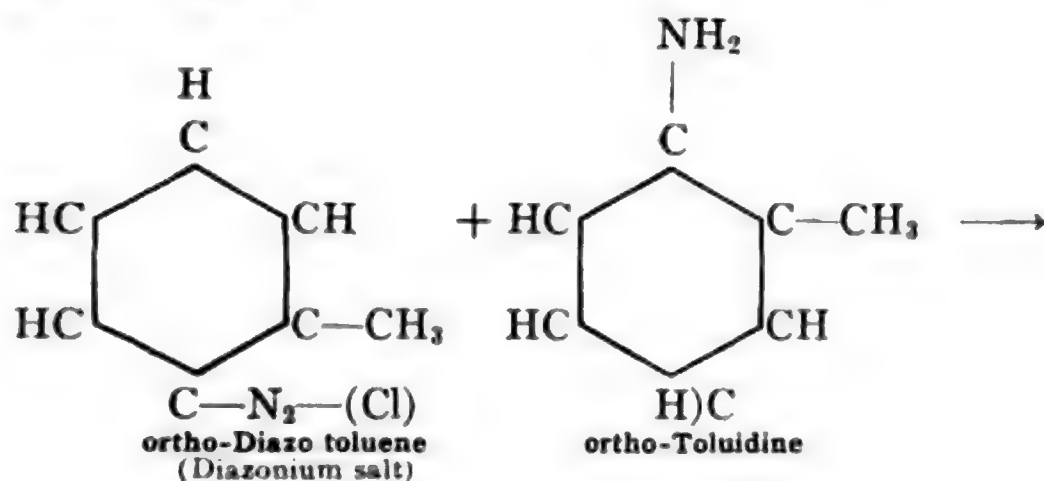
Aminoazo Benzene from Nitroazo Benzene.—Another method of preparing aminoazo compounds is analogous to the preparation of aniline, *i.e.*, by the reduction of the corresponding *nitro* compound. When **azo benzene** is nitrated we obtain **nitro azo benzene** and this on reduction yields **amino azo benzene**.

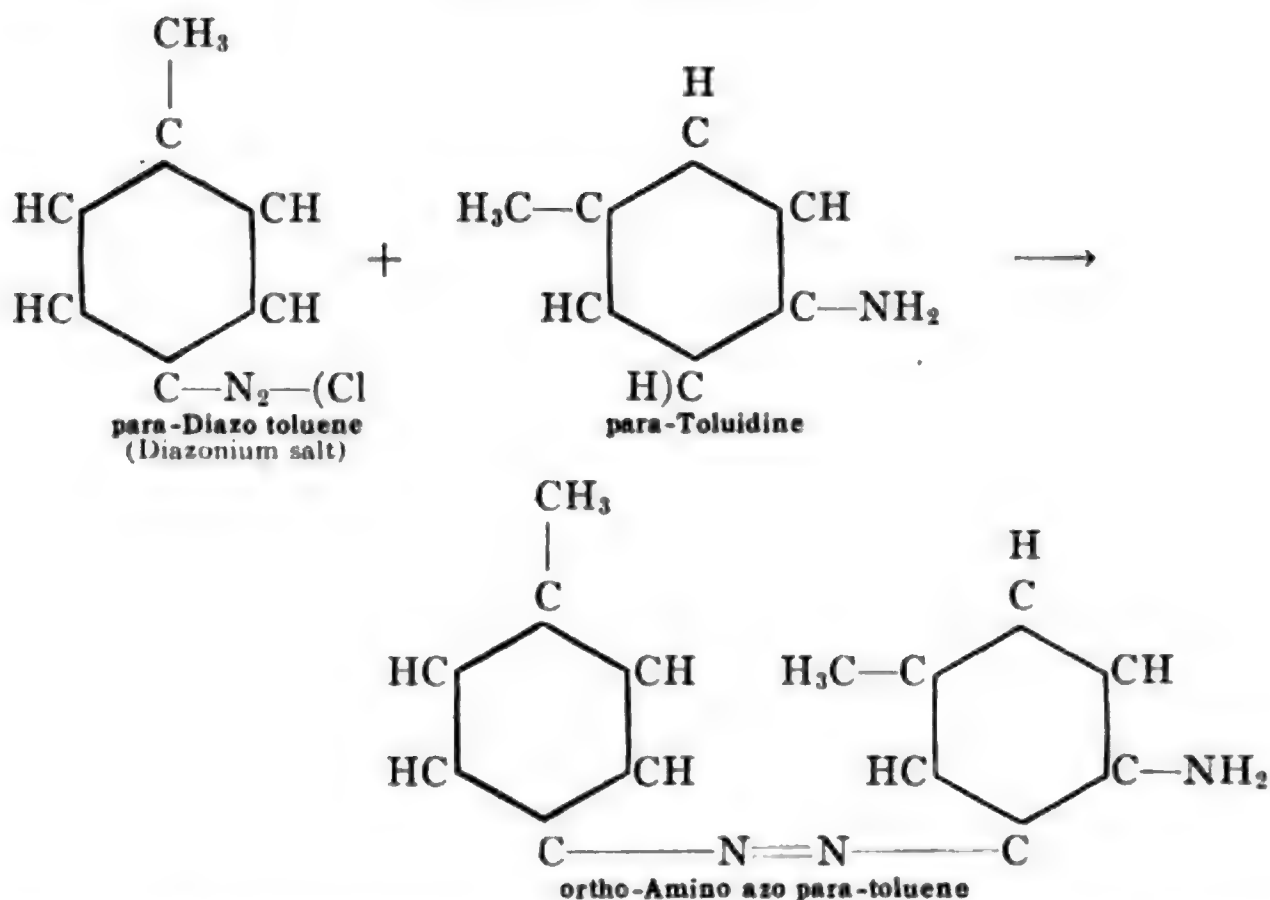


Constitution.—Both of these reactions of preparation establish the constitution of the amino azo compounds and also of the hydroxy azo compounds as we have represented them. While three isomers are possible in each case, depending on whether the azo group and the amino or hydroxyl group are in the *ortho*, *meta* or *para* positions in relation to each other, yet in fact only *ortho* and *para* compounds are known in most instances. The full constitution of the *ortho* and *para* **amino azo benzene** is then,



By the **Griess** reaction the para compound is always formed unless, in the case of the homologues of aniline, *e.g.*, in preparing the **amino azo toluenes**, the para position is occupied. In this case the ortho compound results.



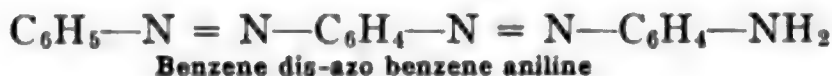


The ortho and para amino azo compounds differ in certain reactions and the view is held by some that two different formulas represent them. We shall not take up the discussion of this question however.

Amino azo compounds are in general yellow or brown crystalline substances insoluble or difficultly soluble in water, but soluble in alcohol or ether. They are basic compounds readily forming salts which usually possess a distinctly different color from that of the free bases. As amino compounds they are able to be diazotized and converted into still more complicated azo compounds in which *two* azo groups are present in the molecule and which are known as *dis-azo* compounds.



These, also, may yield amino and hydroxyl derivatives, *e.g.*;



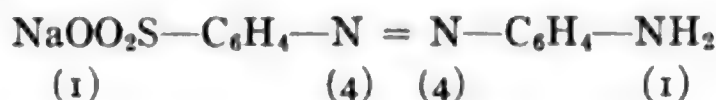
This, again, may be diazotized and then coupled with a new ring yielding a compound containing *three* azo groups and termed a *tris-azo* compound.

The most important derivatives of the amino azo compounds are the sulphonic acids of which *mono-* and *di-sulphonic acids* are known.

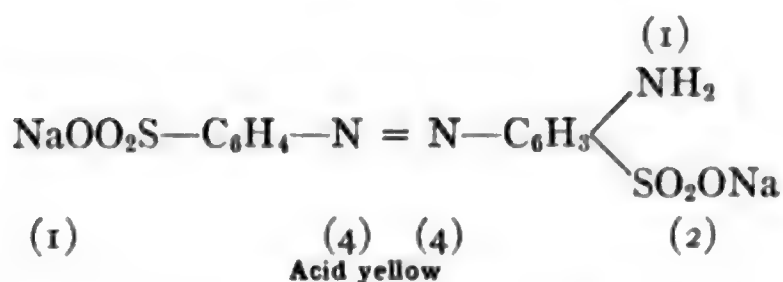
Amino Azo Benzene, $\text{C}_6\text{H}_5\text{—N=N—C}_6\text{H}_4\text{—NH}_2$

This is the simplest amino azo compound and is known in the *para* form. It is a yellow-brown crystalline substance melting at 126° , and boiling at 360° . It is soluble in alcohol and slightly in hot water.

Aniline Yellow.—It is a dye known as **aniline yellow** and is of especial interest in being the *first azo dye* used (1863), though it was first prepared by Griess in 1859, by the reaction just described (p. 570). At present it is not used as a dye to any extent. The hydrochloride salt is a beautiful violet colored substance which dissolves slightly in hot acids to a red colored solution.



and



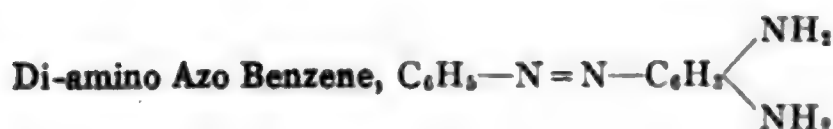
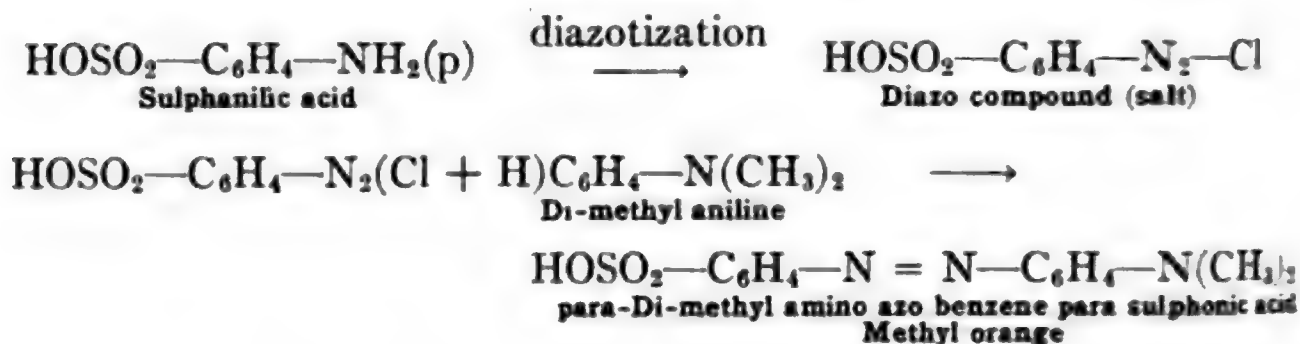
Acid Yellow.—A mixture of the sodium salts of the mono- and di-sulphonic acid derivatives of amino azo benzene is a dye known as **acid yellow** or **fast yellow**, as above.

Di-methyl Amino Azo Benzene, $\text{C}_6\text{H}_5\text{—N=N—C}_6\text{H}_5\text{—N(CH}_3)_2$

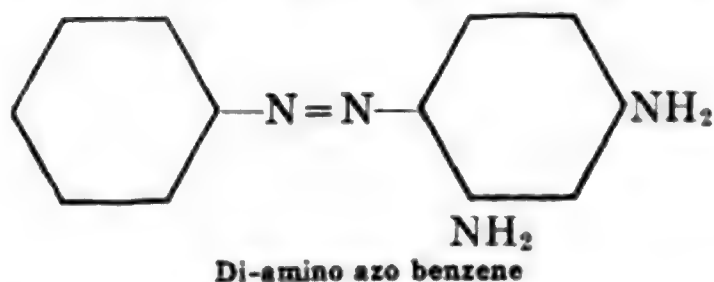
Butter Yellow.—The *di-methyl* derivative of amino azo benzene which we have referred to in our discussion of the general method for the formation of amino azo compounds by the Griess reaction (p. 569), is also a dye known as **butter yellow**. It is insoluble in water, but soluble in oils and, therefore, is used to color butter.

Methyl Orange.—Another important dye compound related to the above is the well-known **methyl orange** which, though not used as a dye, is very widely used as an indicator. It is the *mono-sulphonate* derivative of **di-methyl amino azo benzene**. The alkali salts are orange yellow in color while the free acid is red violet, and these are the colors obtained when the indicator is used in acidimetric titrations.

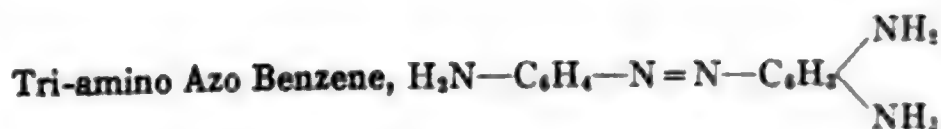
It is known also as **helianthine** and as **tropæolin D**. It is not prepared by starting with amino azo benzene but with **sulphanilic acid** which is **para-amino benzene sulphonic acid**. This is **diazotized** and then coupled with **di-methyl aniline** yielding the azo compound.



Both di-amino and tri-amino azo compounds are known. In these compounds in which two amino groups are in the same ring the azo group cannot be *para* to both and it is found that the most common form is the one in which one amino group is *ortho* and the other *para*.

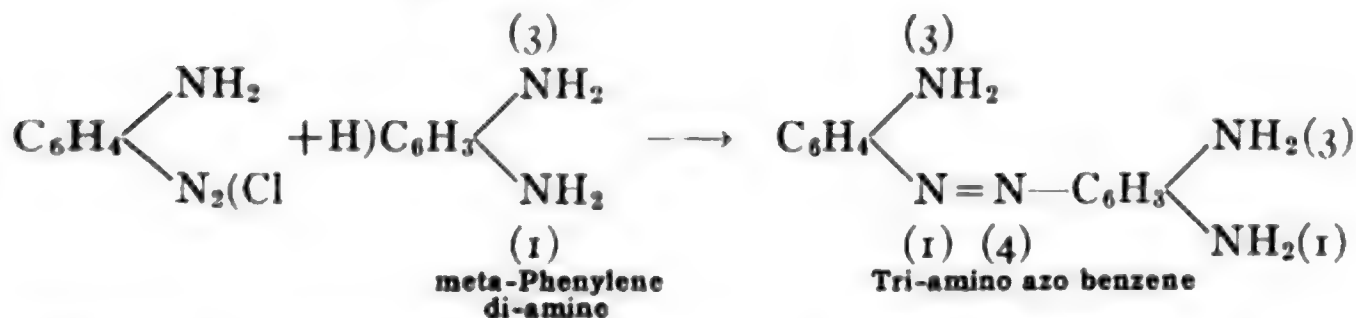
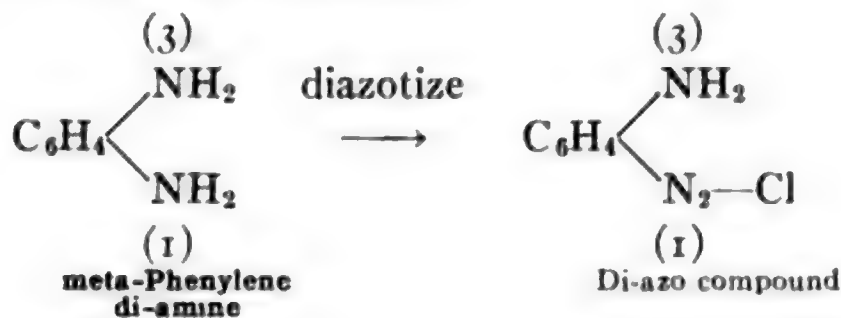


Chrysoidine.—The hydrochloride salt of this compound is a dye known as **chrysoidine**. The mono-hydrochloride salt is yellow while the neutral or di-hydrochloride salt is carmine. The free base crystallizes in yellow needles.

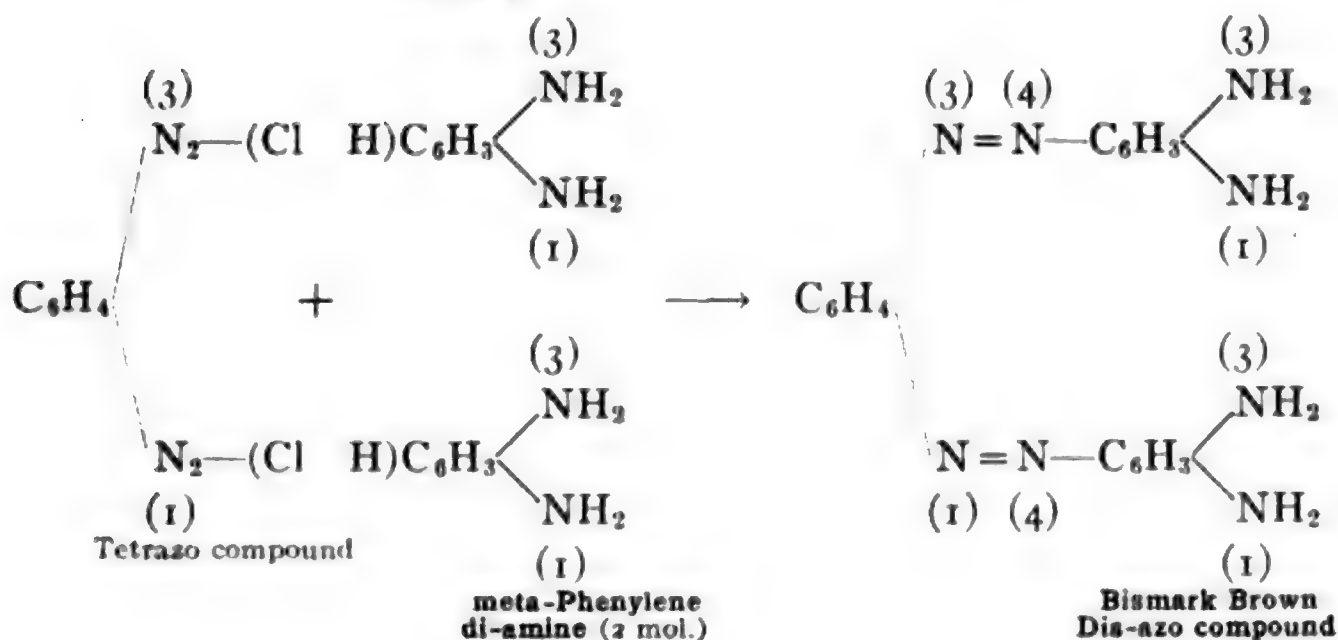
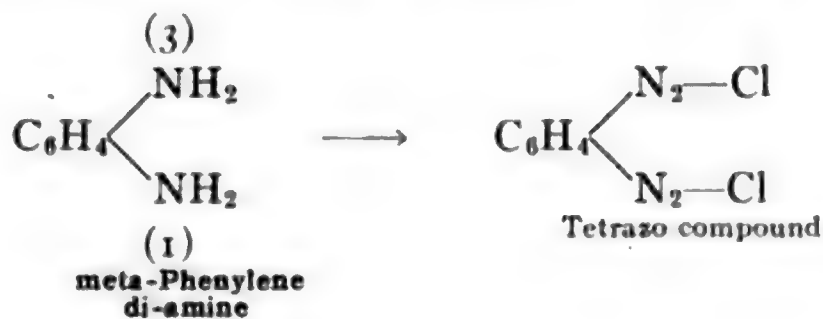


The important *tri-amino azo* compound is the one in which two amino groups are in one ring, *ortho* and *para* to the azo group and one amino group *meta* to the azo group in the other ring. The constitution of the compound is proven by its preparation from **meta-phenylene di-amine**, *meta*-di-amino benzene. This is diazotized so that only one

of the amino groups is diazotized and then coupled with another molecule of the *meta*-phenylene diamine.



When the diazotization of the meta phenylene diamine is carried further so that both amino groups are diazotized a double diazo compound or *tetrazo* compound is obtained and this couples with two molecules of meta-phenylene diamine yielding a double azo or *dis-azo* compound.



Bismarck Brown.—The *dis-azo* compound obtained **meta-di-amino benzene dis-azo benzene meta-di-amino benzene** is a dye known as **Bismark brown**, though the dye is probably a mixture of the *dis-azo* compound and tri-amino azo benzene. With the exception of **aniline yellow** or **amino azo benzene** it was the first azo dye to be made. It was first prepared by **Martius** in 1864, and first made as a dye in 1866.

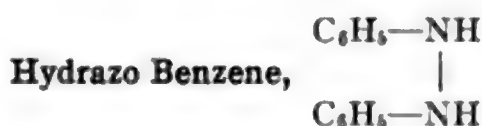
HYDROXY AZO COMPOUNDS

The *hydroxy azo* compounds are wholly analogous to the *amino azo* compounds and much that we have said in regard to the latter applies without exception to the former. The chief difference is that due to the different character of the substituting group. While the amino azo compounds are basic, due to the amino group, and form salts with acids; the hydroxy azo compounds are acid, forming salts with bases. The acid character is due to the aromatic hydroxyl group which, as we shall presently show, is strongly acid. In general the hydroxy azo compounds are yellow or brown in color and the azo dyes formed from the simpler hydroxy azo compounds possess the same general color and are mostly yellow, orange or red with a few blue and black dyes. While many of the first azo dyes made are amino azo compounds it is interesting that now the hydroxy azo compounds are far more important. It is also a striking fact that while many of the *amino azo* dyes are derivatives of benzene and its homologues the important **hydroxy azo** dyes are not derivatives of benzene or its homologues, but of **naphthalene** which is a hydrocarbon of another class and which will be studied later. The consideration of the dyes of this type will, therefore, be taken up in connection with this new class of hydrocarbons.

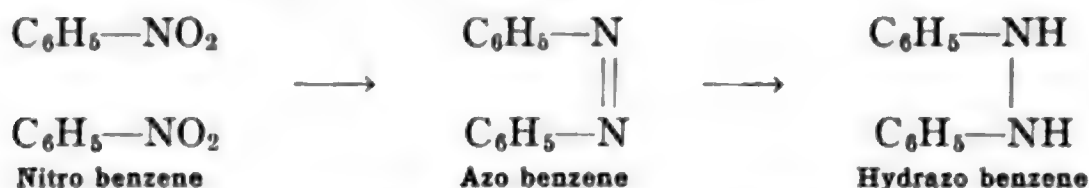
Azo Dyes.—Enough has been said in the preceding discussion of the *azo* compounds, including *amino azo* and *hydroxy azo* derivatives to indicate their importance in the *dyestuff industry*. When we consider the great variety of derivatives and complicated products which can be made, we may form some idea, even without further elaboration, of the importance of this large group of compounds which universally possess strong color, usually a different color in the free base or acid and in the salt, and which have been found to possess the peculiar character necessary to their use in dyeing fabrics. The relation between chemical constitution and the property of color and of dyeing

fabrics will not be considered as it belongs to a more special treatment of dyes as a class. In our study we are concerned only with the chemical constitution and relationship of the individual chemical compounds

HYDRAZO COMPOUNDS



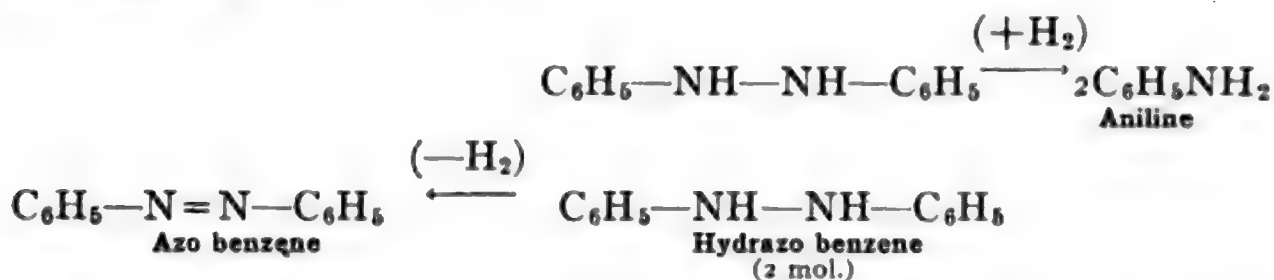
When **azo benzene** is reduced or when the reduction of **nitro benzene** is continued beyond the stage of the azo compound we obtain **hydrazo benzene**, a colorless crystalline solid, m.p. 126°. The reduction may be accomplished (1) by using zinc and alcoholic sodium hydroxide, (2) by means of an alcoholic solution of ammonium sulphide or (3) electrolytically in the presence of an alkali.



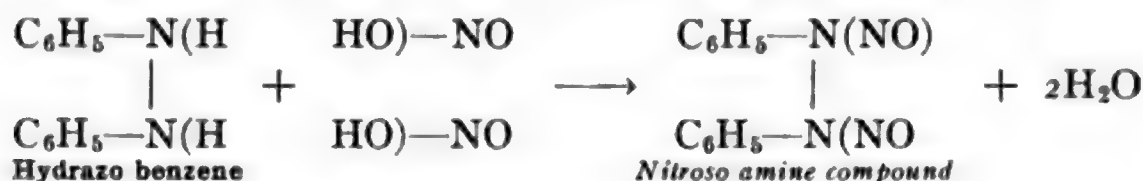
The characteristic difference in the constitution of *azo* compounds and *hydrazo* compounds is that in the azo compounds the two aromatic rings are linked by two nitrogen atoms which are themselves *doubly linked to each other*; while in the hydrazo compounds the nitrogen atoms linking the two rings together are singly linked to each other, the remaining valence of each trivalent nitrogen being satisfied by an additional hydrogen atom. Just as these two benzene compounds are successive reduction products of nitro benzene so also, as they yield aniline on further reduction (p. 537), they may be considered, in the reverse order, as successive oxidation products of aniline. Thus the two nitrogen atoms of the azo compounds and the two (NH) groups of the hydrazo compounds are residues of *amino* groups. As in the azo compounds so also in the hydrazo the two rings may be alike giving symmetrical compounds, or they may be unlike giving unsymmetrical.

Oxidation and Reduction.—Hydrazo compounds are usually colorless crystalline substances insoluble in water, but soluble in alcohol. They oxidize easily, even in the air, yielding the azo compound, and on reduction yield the amino compound. At high temperatures they often undergo a reciprocal oxidation and reduction of two molecules one being oxidized at the expense of the other which is thereby reduced.

Thus **hydrazo benzene** reacts with itself and yields both **azo benzene** and **aniline**.

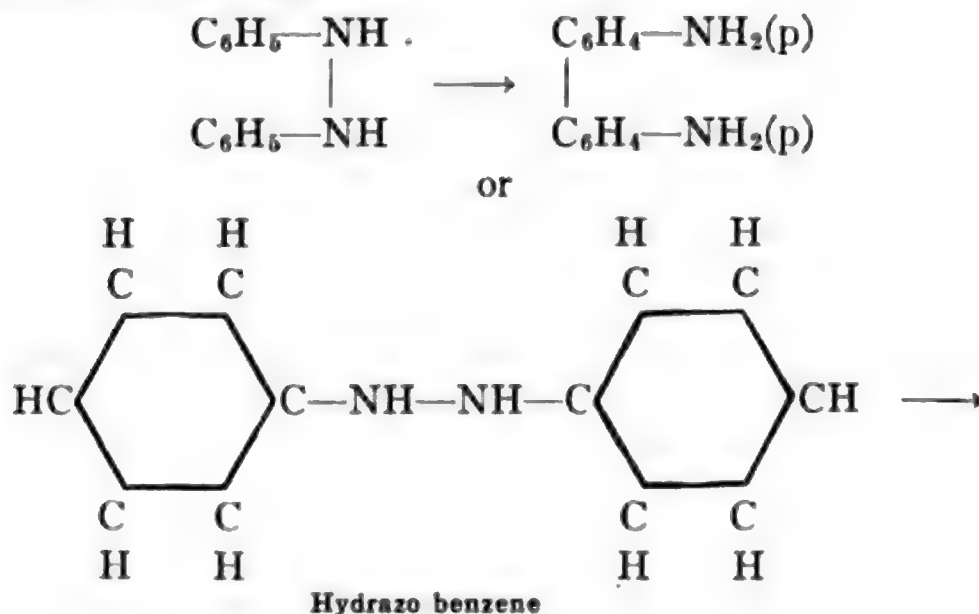


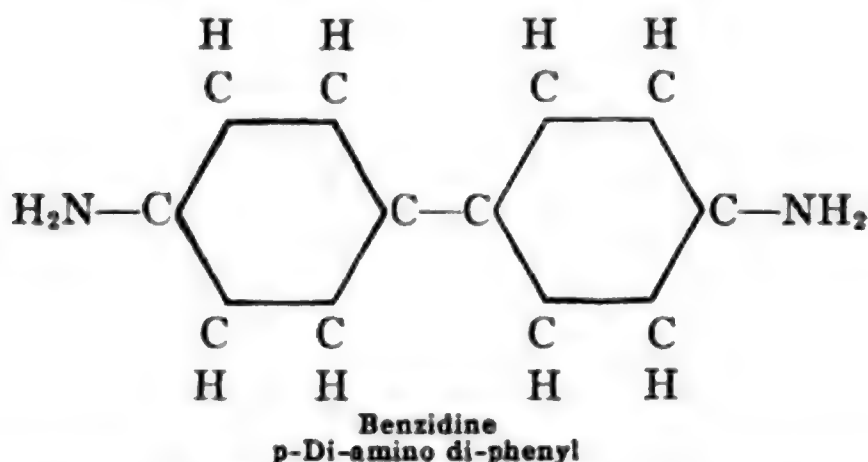
Secondary Amines.—Like *secondary* amines the hydrazo compounds contain the (NH) group and toward nitrous acid hydrazo benzene reacts at low temperatures in the manner characteristic of this class of amines (p. 61) and yields a double nitroso amine compound.



Molecular Rearrangement.—Like several of the other nitrogen compounds which we have been studying, hydrazo benzene undergoes a molecular rearrangement resulting in a compound in which the two rings, instead of being linked by means of nitrogen groups, become directly linked to each other, the two *imino* nitrogen groups becoming two *amino groups* in the *para* position to the linkage of the rings.

Benzidine.—The compound formed is known as **benzidine**, and is a di-amino derivative of a hydrocarbon consisting of two benzene rings directly linked together, known as di-phenyl. Both of these will be considered later (p. 730).



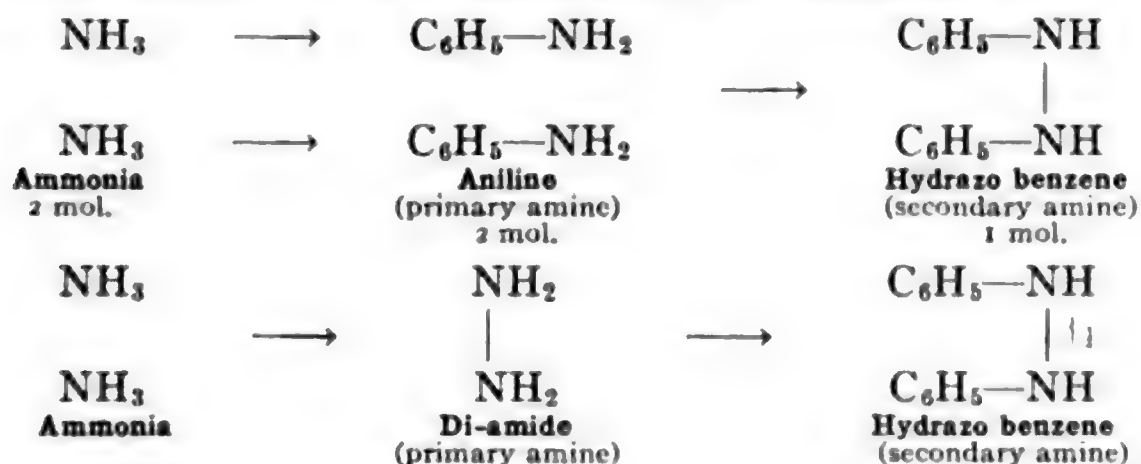


The compound formed like those in similar rearrangements is the *para* compound, *i.e.*, the linking of the rings occurs in the position *para* to the amino groups. If, in the case of derivatives of hydrazo benzene, the position *para* to the nitrogen link is occupied then the direct linking of the rings occurs in the position *ortho* to the amino groups. The rearrangement in the case of hydrazo benzene is accomplished by simply boiling with mineral acids.

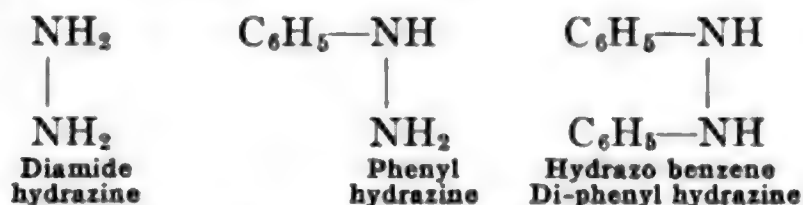
Benzidine Dyes.—The importance of hydrazo compounds in connection with dyes is not on their own account for, as has been stated, they are colorless compounds; but because they are easily oxidized to azo compounds which are dye compounds and because of the above rearrangement into compounds like **benzidine** which yield dyes known as **benzidine dyes** (p. 787).

HYDRAZINES

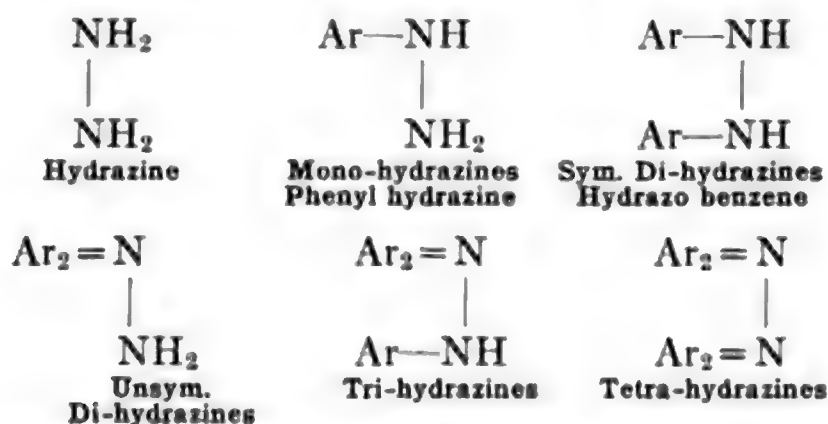
Derivatives of Di-amide.—We have discussed the relationship of hydrazo benzene to aniline and just as aniline is a derivative of one molecule of ammonia so hydrazo benzene may be considered as a derivative of two molecules of ammonia or better as a derivative of **di-amide** (p. 64), which is itself derived from two molecules of ammonia by the substitution of an *amino* group into **ammonia** itself.



As a derivative of **diamide**, however, another compound is more important than hydrazo benzene. This is known as **phenyl hydrazine**, and it stands intermediate between diamide and hydrazo benzene. Just as dibasic acids form not only *neutral salts* and *neutral amides*, but also *acid salts* and *acid amides* by the replacement of one acid hydrogen by a metal or *one* acid hydroxyl by the amino group; so diamide being a *di-amine* yields not only derivatives in which the *two* amino groups each have a hydrogen replaced by a radical but also intermediate compounds resulting from the substitution of a hydrogen in only *one* amino group. Such an intermediate phenyl derivative of **di-amide** we shall now study. As diamide is known also as **hydrazine** its phenyl derivative is known as **phenyl hydrazine**.



Hydrazines.—It will readily be seen that these two compounds are not the only *aromatic* (*aryl*) derivatives of di-amide or hydrazine. The following series is possible; the *aryl* radical, when more than one is present being either like or different.



All of these compounds are termed **hydrazines** although the symmetrical di-hydrazines retain the name of **hydrazo** compounds because of their relationship to the azo compounds.

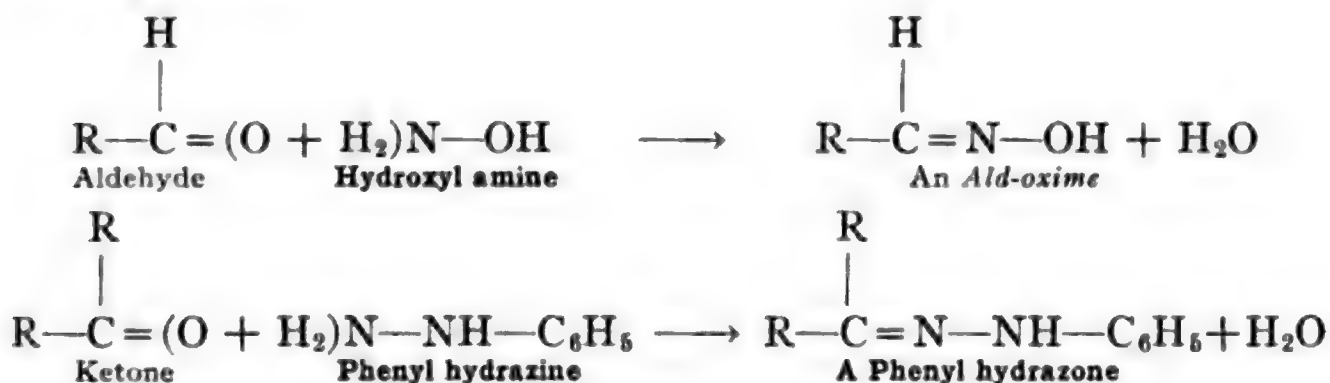
Phenyl Hydrazine, $\text{C}_6\text{H}_5\text{—NH—NH}_2$

Phenyl hydrazine is by far the most important of the hydrazine compounds. It is a colorless oil readily becoming dark colored. It melts at 17.5° and boils at 243.5° . It forms a crystalline hydrate, m.p. 24.1° , with $1/2$ mol. H_2O , $\text{C}_6\text{H}_5\text{—NH—NH}_2 \cdot 1/2\text{H}_2\text{O}$. As it

contains a primary amine group it possesses basic properties yielding soluble crystalline salts, *e.g.*, $\text{C}_6\text{H}_5\text{—NH—NH}_2\cdot\text{HCl}$, **phenyl hydrazine hydrochloride**.

Carbohydrate Reagent.—The importance of phenyl hydrazine rests upon its use as a reagent in the study of the **carbohydrates** and other *aldehyde* or *ketone* compounds. The reaction, together with the analogous one of **hydroxyl amine**, has been fully discussed in Part I, p. 326, but may be repeated in this connection. It is based upon the

characteristic property of the *carbonyl group*, —C=O , in aldehydes and ketones to react with an amino group containing two unsubstituted hydrogen atoms.

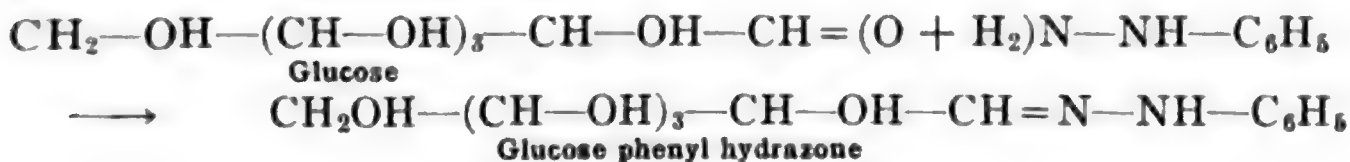


The products are known as *oximes*, from hydroxyl amine and **hydrazones** from the hydrazine. Phenyl hydrazine yields **phenyl hydrazones** of the particular aldehyde or ketone with which it reacts. The reaction is of value in connection with the carbohydrates because these react as aldehyde or ketone compounds and because the hydrazones formed undergo further reaction with phenyl hydrazine.

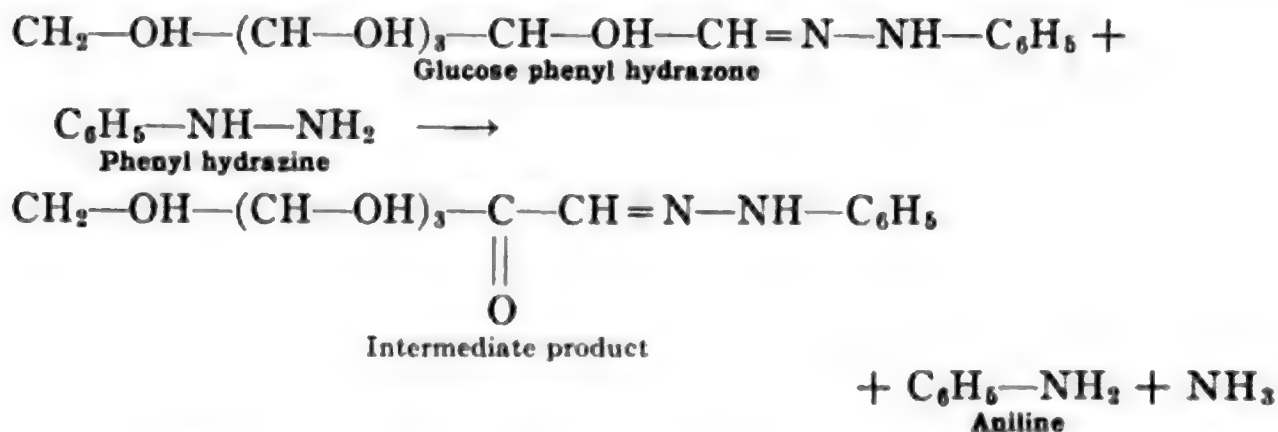
Oxidizing Agent.—This subsequent reaction with phenyl hydrazine is due to its action as an oxidizing agent. If the reduction of the phenyl hydrazine is brought about by hydrogen, zinc and hydrochloric acid, the products are aniline and ammonia.



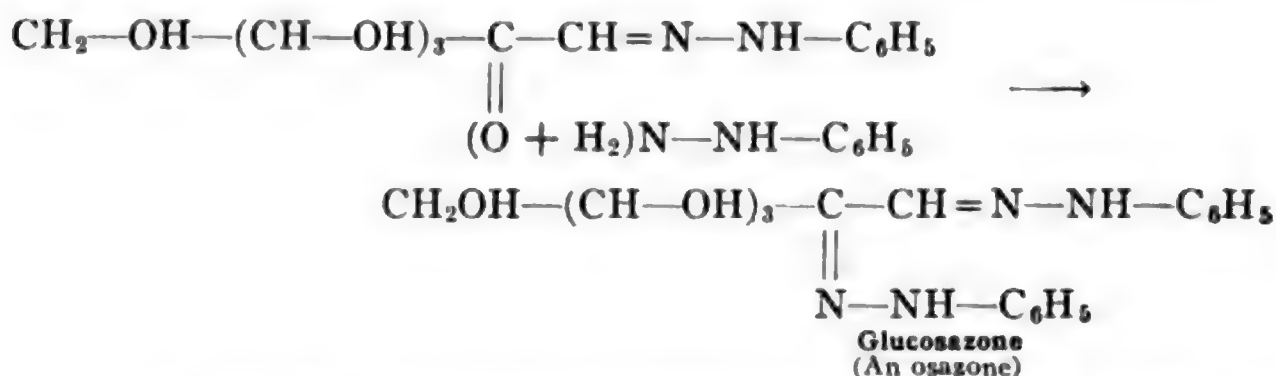
This same reduction of phenyl hydrazine occurs when it acts as an oxidizing agent upon the hydrazone formed by the reaction between glucose and phenyl hydrazine.



On this glucose phenyl hydrazone the phenyl hydrazine acts as an oxidizer and one of the *secondary alcohol* groups ($-\text{CH}-\text{OH}-$) is oxidized to a ketone carbonyl group, the phenyl hydrazine being reduced as above to aniline and ammonia.



Osazones.—The intermediate product thus formed containing now a carbonyl group reacts with a third molecule of phenyl hydrazine forming a *di-hydrazone* which is termed an **osazone**.



The osazones are crystalline products able to be separated and identified, and furthermore by hydrolysis they split off both phenyl hydrazine radicals yielding an aldehyde-ketone product of the original glucose known as an *osone*, i.e., **glucosone**. This by reduction yields the ketone sugar corresponding to the original aldehyde sugar with which we started (p. 328).

Reducing Agent.—Phenyl hydrazine may also act as a reducing agent. *Nitro* and *nitroso* compounds are reduced by it to *amino* compounds the phenyl hydrazine being oxidized to **benzene**. Phenyl hydrazine also yields benzene when oxidized by ferric chloride or Fehling's solution, the nitrogen being set free quantitatively thus giving a means of determining the amount of hydrazine present.

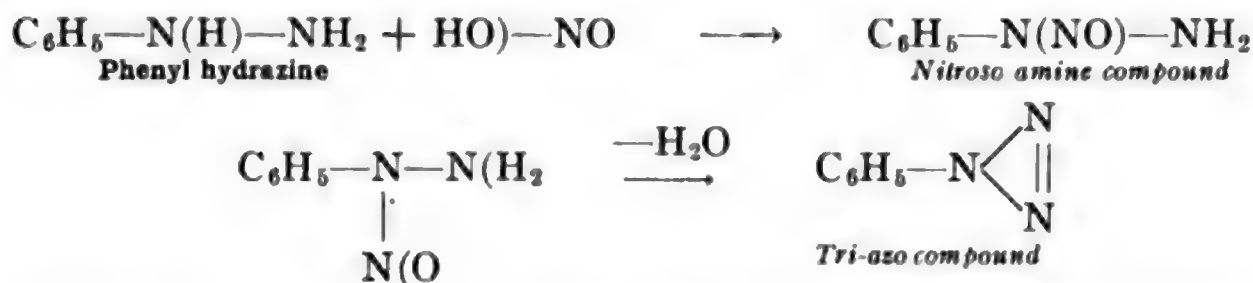


By more cautious oxidation with mercuric oxide, copper sulphate or ferric chloride, the salts of phenyl hydrazine yield salts of **diazo benzene**.



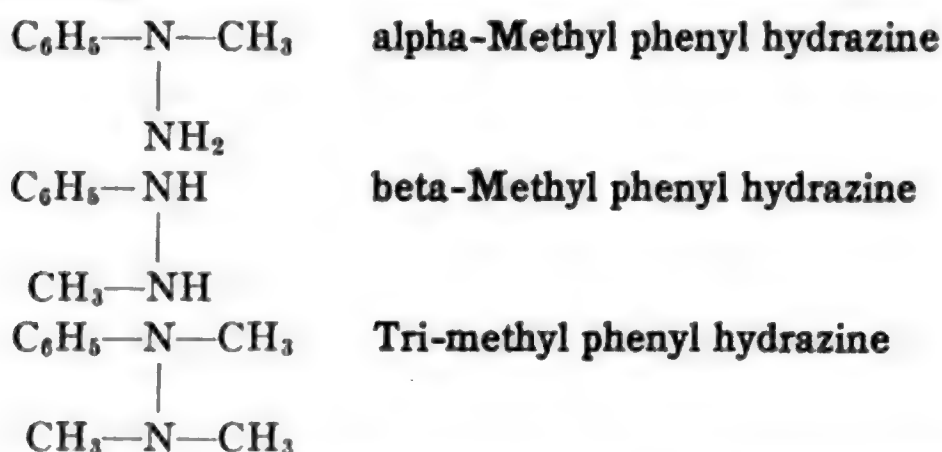
Conversely benzene diazonium chloride by reduction with zinc and acetic acid yields phenyl hydrazine.

Tri-azo Compounds.—As phenyl hydrazine is both a *primary* and a secondary amine the (NH) group reacts with nitrous acid yielding a *nitroso amine* compound. This compound is very unstable, readily losing water, and forming a compound in which the ring is linked to a three nitrogen group. It is known consequently as a *tri-azo* compound, also as a *diazo imide*.

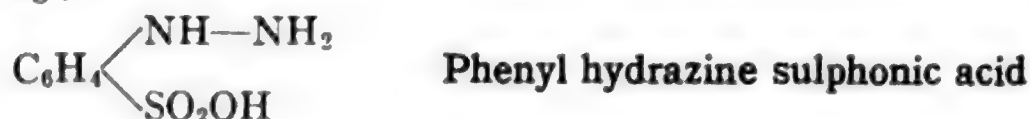


This triazo compound is a derivative of the interesting *nitrogen-hydrogen* acid, N_3H , **hydrazoic** or **triazic acid**, (p. 64).

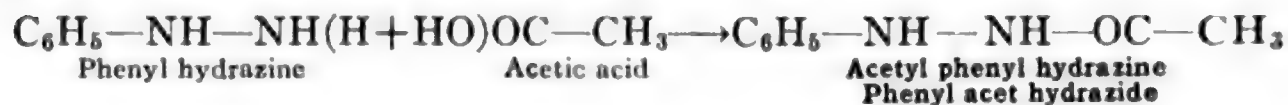
Derivatives.—Four classes of derivatives of phenyl hydrazine are known; (1) Those containing hydrocarbon radicals in place of amino hydrogen atoms,



These correspond to the di-, tri-, and tetra-hydrazines previously mentioned. (2) Derivatives containing a substituting group in the ring, *e.g.*;



(3) Derivatives of the *acid amide* type in which phenyl hydrazine, as an amine, reacts with carboxyl acids or acid chlorides.



These products are termed *hydrazides*.

(4) Derivatives of the *amino acid* type in which phenyl hydrazine, as an amine, is substituted for a hydrogen atom of the hydrocarbon radical of an acid. They are known as *hydrazino acids*, e.g.;



In both of the last two derivatives either one of the *primary* or the *secondary* amine hydrogen may be replaced.

VI. DI-AZO COMPOUNDS.

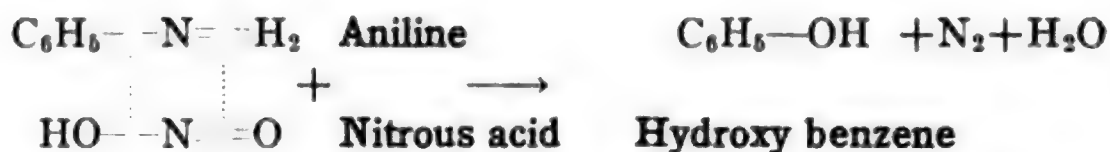
In the preceding discussion of the aromatic nitrogen compounds we have repeatedly referred to the *diazo* compounds and to certain reactions which they undergo especially those by which they yield azo compounds (p. 569). The general formula for diazo compounds, $R-N_2-X$, differs from those for *azo* compounds, $R-N=N-R$, and hydrazo compounds, $R-NH-NH-R$, in that only *one* of the two nitrogen atoms is linked directly to a ring. The number of atoms of nitrogen in proportion to one aromatic ring being *two*, whereas in azo compounds it is *one*, explains the name *di-azo*.

The diazo compounds are characterized also by their great instability which is evident in the explosive nature of the dry salts and in the great ease with which they undergo reaction when in solution. It is this last fact which enables them to be used in the laboratory and in industrial operations for the preparation of many valuable compounds, especially dyes. No class of compounds in the whole field of organic chemistry has been so rich in the yield of important products, or so widely applicable as a means, either direct or indirect, of bringing about certain desired results. Their discovery is one of the important landmarks in the history of organic chemistry and the developments resulting from it both in the science of chemistry and in the industries have been comparable with those resulting from the discovery of the mother substance **coal tar**.

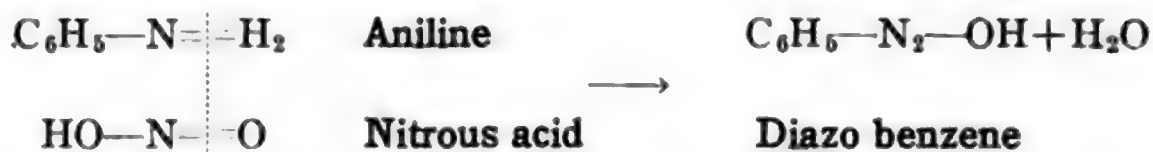
Diazo compounds are soluble in water, but practically insoluble in alcohol or ether. On account of their explosive nature when dry they are seldom obtained in any amount as the pure dry product. When necessary to isolate the pure compound, only very small quantities, 0.1 to 0.2 g. are ever separated. It is usually unnecessary to isolate the compounds as such, as they are simply intermediate steps in the preparation of other compounds resulting from their decomposition by different reagents. Therefore they are held in the solution in which they are prepared and decomposed at once. Details in regard to amount of reagent used, the regulation of the temperature during the reaction, thorough stirring, etc., must oftentimes be carefully observed

if successful results are to be obtained. These will not be taken up here, but may be found in descriptions of laboratory methods for special cases. The study and use of these exceedingly unstable compounds has shown in a remarkable way the difficulties and triumphs of laboratory and industrial technique.

Peter Griess, 1858.—Diazo compounds were discovered and first prepared by **Peter Griess** in 1858. The historical method used by him is the same in general as is now used widely in dyestuff manufacture. It has already been described and consists in the action of *nitrous acid* on an *aromatic primary amine*, e.g., **aniline**. When this reaction takes place, at ordinary or slightly raised temperatures, the same products are obtained as with aliphatic primary amines, viz., the *hydroxyl compound* of the hydrocarbon radical, free *nitrogen* and *water*.



When, however, the reaction takes place in the cold an aromatic amine yields the intermediate *diazo compound*.

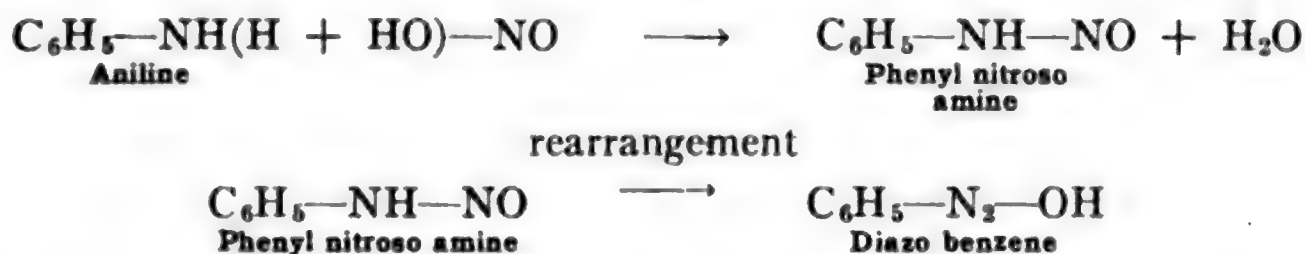


The details of this reaction and the one following will be considered later in discussing the constitution of diazo compounds. The reaction always takes place in an acid solution, *i.e.*, with the salt of the amine, so that the product obtained is not the diazo benzene as written above, but the salt of it.

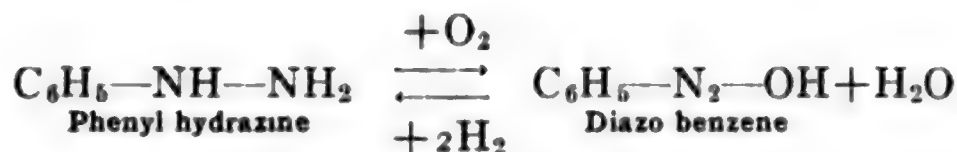


Diazotization.—The reaction is termed *diazotization*, *i.e.*, we *diazotize* the amine. These terms are now of every-day use in the synthesis of organic compounds and are similar and almost as familiar as the terms oxidation and oxidize. While the principle of diazotization and the general reaction is as given above there are various modifications that have been introduced. Originally the nitrous acid for the diazotization was prepared in the presence of the amine by passing

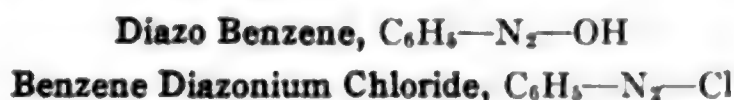
nitrogen trioxide gas, N_2O_3 , into the water solution of the amine salt, the nitrogen trioxide being prepared by the action of arsenious oxide, As_2O_3 , upon nitric acid. At present this procedure is rarely followed; but instead **sodium nitrite**, $NaNO_2$, is added to an acid solution of the amine salt. In both cases the diazo compound is obtained as a water solution of the diazonium salt which must usually be kept cold in order to prevent decomposition. If it is desired to obtain the diazonium salt as a crystalline product in alcohol, then, instead of sodium nitrite, we use either **amyl nitrite**, $(CH_3)_2=CH-CH_2-CH_2-NO_2$, or **ethyl nitrite**, $C_2H_5-NO_2$ (p. 104). These nitrites with acids yield nitrous acid. The result then of all of the procedures for diazotization is the bringing together of *free nitrous acid* and the salt of an *aromatic primary amine*, the reaction between these two taking place as described. It is considered probable by some that the diazo reaction takes place in two steps, first, the formation of a *nitroso amine compound*, as in the case of secondary amines with nitrous acid and, second, the rearrangement of this nitroso amine into the diazo compound.



Diazo compounds may also be prepared from **hydrazines** by cautious oxidation with mercuric oxide, copper sulphate or ferric chloride (p. 583).



The reverse reaction also takes place on reduction if the diazonium salt, usually the sulphite, is reduced by means of zinc and acetic acid.



Constitution.—In the following discussion of the constitution and reactions of diazo compounds **diazo benzene** and its salts will be taken as examples. The reactions, however, are to be considered as typical of all diazo compounds. The physical properties of free diazo com-

pounds are known in only a few cases because the study of them is attended with both difficulties and dangers. **Diazo benzene**, to which we give the formula $C_6H_5-N_2-OH$, has never been obtained as such. It is formed in solution when moist silver oxide acts upon the chloride salt of diazo benzene. It acts as a base but rapidly decomposes.

Bases, Neutral Salts.—As a base it forms salts, in which form the diazo compound is obtained by diazotization, and which though also unstable has been isolated in small quantities and the composition and properties determined. Of the three salts, the *sulphate*, *chloride* and *nitrate*, the first is the most stable and the last is the least stable. They are colorless crystalline *neutral* compounds soluble in water, difficultly soluble in alcohol and insoluble in ether. After being prepared by the ordinary diazo reaction, with sodium nitrite in cold acid water solution, they may be precipitated in crystalline form by the addition of alcohol and ether. If the diazotization is effected in alcohol solution by means of **amyl nitrite** or **ethyl nitrite** the crystals of the diazonium salt separate at once. These salts of diazo benzene all show true salt characteristics, *e.g.*, they lower the freezing point of solutions. The diazo radical, $(C_6H_5-N_2-)$ is thus basic toward strong acids, and the hydroxide, the non-isolated hypothetical diazo benzene, $C_6H_5-N_2-OH$, is the free base. It may be considered as the simplest aromatic diazo compound and the mother substance of all other members of the class.

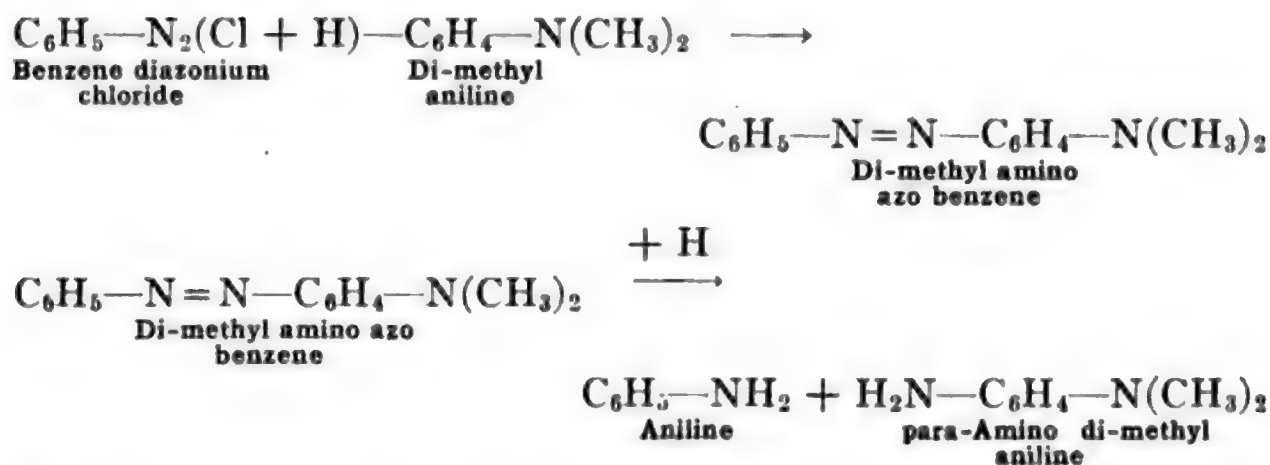
What now is the constitution of these diazo compounds? The facts thus far considered and which must be explained by an accepted constitutional formula are, (1) Their *formation* by the action of nitrous acid on a primary amine, (2) Their conversion into *azo*, *amino azo*, *hydroxy azo* and *hydrazine* compounds and (3) the *basic* character of the hydroxy compound, **diazo** benzene, and the true *salt* character of the compounds formed with strong acids.

Griess Formula.—Historically interesting is the first formula proposed by **Griess**. Because of the *ammonium* salt-like character of the salts of diazo compounds he assumed that the formula for benzene

diazonium chloride was, $C_6H_5-N''' = \overset{v}{N} \begin{array}{l} \nearrow H \\ \searrow Cl \end{array}$, one of the nitrogen atoms

being pentavalent as in ammonium chloride. In this formula each nitrogen is linked to the ring, a condition which was disproved by

the fact that a tetra-brom sulphonic acid derivative of aniline yields a diazo compound in which the four bromine atoms and the one sulphonic acid group remain unchanged; the diazo nitrogen group being thus attached to the ring at one point only, where the original amine group was situated. This was also supported by the fact that in azo compounds, which are readily formed from the diazo, only *one* nitrogen is linked to the original benzene ring. This is proven by the decomposition of **di-methyl amino azo benzene**, formed from **benzene diazonium chloride** and **di-methyl aniline**, which on reduction splits into aniline and *para* **amino di-methyl aniline**.

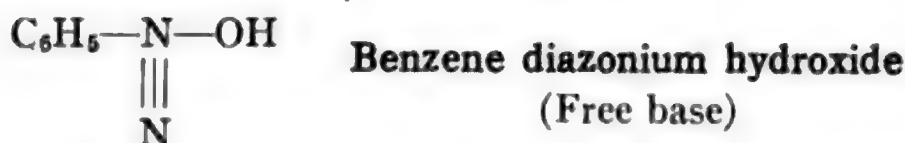
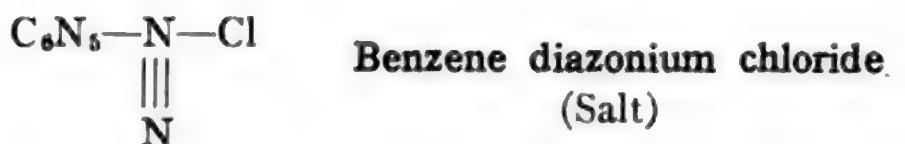


The idea that the diazo nitrogen group is attached to the ring by only one nitrogen and at only one point is further supported by many of the reactions of diazo compounds which result in the replacement of both of the nitrogen atoms by one element or group linked to the ring at only one point, and this is in the position originally occupied by the amino radical of the primary amine from which the diazo compound was formed.

Kekulé Formula.—These facts led **Kekulé** to suggest a second formula in which the nitrogen atoms are both trivalent and in the same relationship to each other and the ring as they are in azo benzene. The formula is $\text{C}_6\text{H}_5\text{—N=N—Cl}$, **benzene diazonium chloride**. For some time this was the accepted formula; for, if we put it in the reactions which we have written for the formation of diazo compounds and for their conversion into azo compounds and into hydrazines, we find that it is satisfactory. It does not agree, however, with the true salt character of benzene diazonium chloride nor the strongly basic nature of the hydroxide compound, the free diazo benzene. In every respect the neutral salts, *e.g.*, benzene diazonium chloride and the free diazo

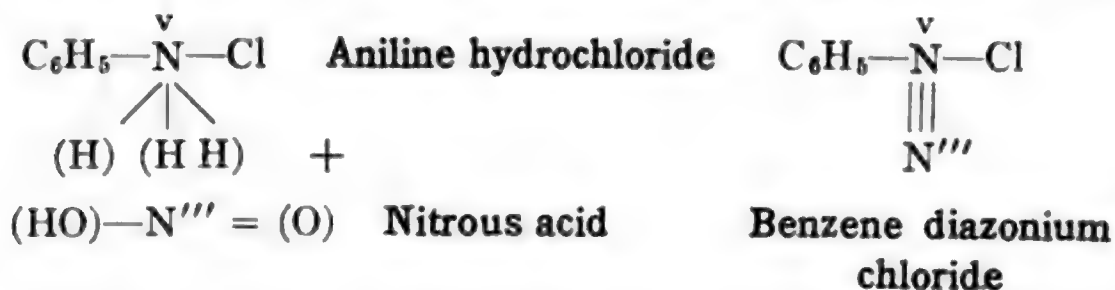
base, resemble ammonium salts and ammonium hydroxide. As in these latter compounds nitrogen is pentavalent so in the diazo salts and base one nitrogen atom, evidently the original amino nitrogen, must be pentavalent. This was partially accounted for in the original **Griess** formula but this we have seen is not in agreement with facts.

Bloomstrand, Strecker and Erlenmeyer Formula.—These ideas resulted in the suggestion of a formula known as the **Bloomstrand-Strecker-Erlenmeyer** formula for the salts and the free base which is as follows:



Bloomstrand-Strecker-Erlenmeyer formulas.

This new formula agrees better with the formation of diazo compounds, for in diazotizing it is always necessary to use, not the free amine, but the *salt* of the amine. The **Kekulé** formula fits the case only if the reaction is written with the amine itself. If, however, we write the reaction with the ammonium-like salt of the amine we find that an ammonium-like salt will naturally result thus agreeing with the facts.



Such a reaction agrees perfectly with the new formula which has been generally accepted as expressing the constitution of the free diazo base and the salts. The base thus takes the name **benzene diazonium hydroxide** and the salts, *e.g.*, the chloride, **benzene diazonium chloride** signifying their *ammonium* character. The new formula does not, however, fit the reactions by which diazo compounds are converted into azo or amino azo compounds nor the reduction of diazo benzene to phenylhydrazine. Thus we have two formulas neither of which

explains all of the three sets of facts mentioned (p. 588), but both of which explain two of them.

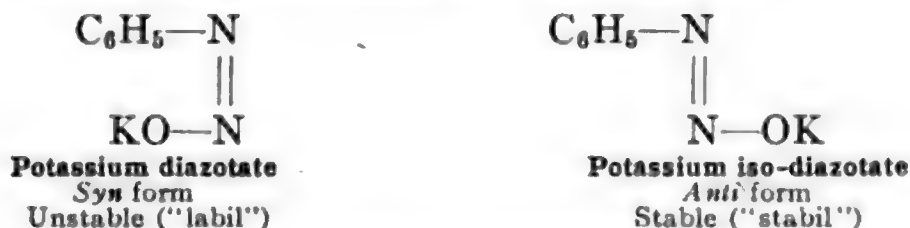
Tautomerism.—We have evidently then another example of *tautomerism* as both formulas are necessary in order to explain the facts and both are true under certain conditions. This has been well supported by some additional facts which favor the **Kekulé** formula, but which also show that both formulas must be true.

Acids, Alkali Salts.—The free diazo benzene base which will always be spoken of now as **benzene diazonium hydroxide** and which necessitates the introduction of the pentavalent nitrogen formula is formed by the action of silver hydroxide upon **benzene diazonium chloride**. By the action of acids the diazonium hydroxide is converted into salts and these salts are *neutral*. If, however, the diazonium chloride is treated with alkalies, like potassium hydroxide, we obtain alkali metal salts of the diazo compound.

Diazotates. Isomerism.—These salts are called *diazotates*, are alkaline, and are not quite so unstable as the *neutral diazonium* salts. They are crystalline compounds, soluble in water and alcohol, but insoluble in ether. By the action of acids they yield the neutral diazonium salts. Again, if a hot strong alkaline solution is used an isomeric salt called an *iso-diazotate* is obtained which is a *stable* compound. According to our ideas it is impossible to conceive of a compound of the constitution of the diazonium hydroxide, like ammonium hydroxide, which is acid in character. There must then be two hydroxide compounds of diazo benzene: **benzene diazonium hydroxide**, a pentavalent nitrogen base, and a tautomeric compound which is called **benzene diazo hydroxide**, and which is *acid* in character. The two are transformable into each other under conditions usually effecting tautomeric change. The diazonium compounds agree with the **Bloomstrand-Strecker-Erlenmeyer** formula. The **benzene diazo hydroxide** should then agree with the tautomeric **Kekulé** trivalent nitrogen formula. Does this formula, however, fit the case of the *isomerism* of the diazotates which we have mentioned?

Hantzsch Stereo Formula.—A development of the **Kekulé** formula to agree with the existence of isomeric diazotates was suggested by **Hantzsch**. He assumed *geometric stereo-isomerism*, due to the double linking of two nitrogen atoms, and this assumption has been supported not only by the isomerism of the diazotates, but also of other similar

nitrogen compounds. The **Kekulé** formula then as developed by **Hantzsch** for the two isomeric **potassium diazotates** is:



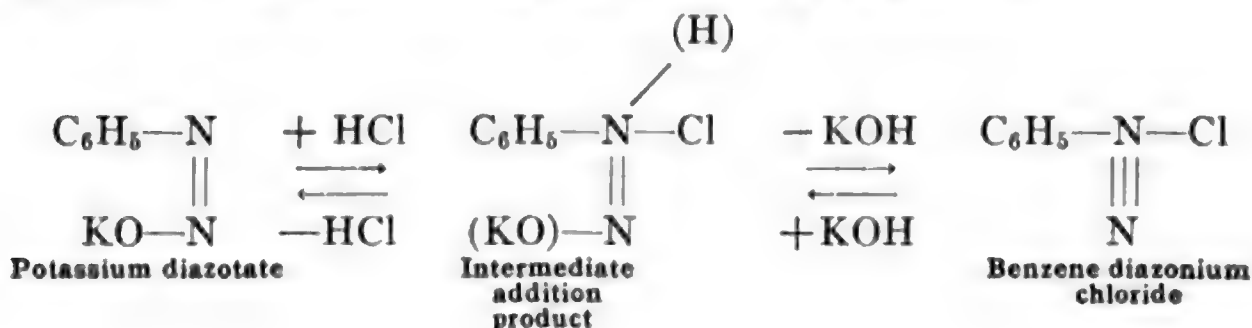
Kekulé-Hantzsch formulas

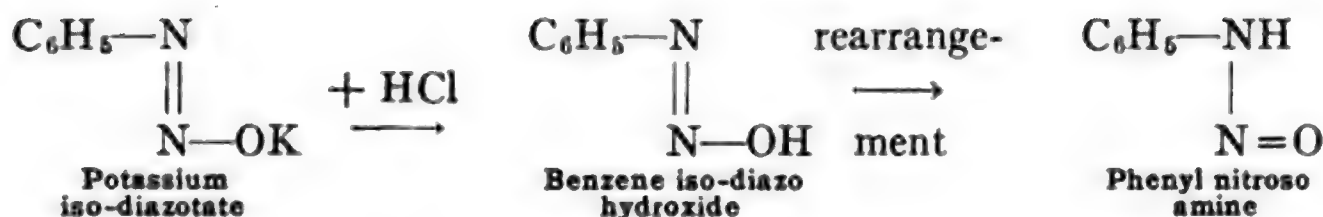
Syn. Anti.—This isomerism is *geometric*, as the double link of the two nitrogen atoms prevents free rotation and the structure of each form will remain fixed. The two forms are termed *syn* when the ring and the other group are on the same side of the nitrogen atoms and *anti* when they are on opposite sides. The condition is exactly analogous to that in **maleic acid** and **fumaric acid** in which two carbon atoms are similarly doubly linked. The terms *syn* and *anti*, for the diazotates, are analogous to *cis* and *trans* for maleic and fumaric acids.



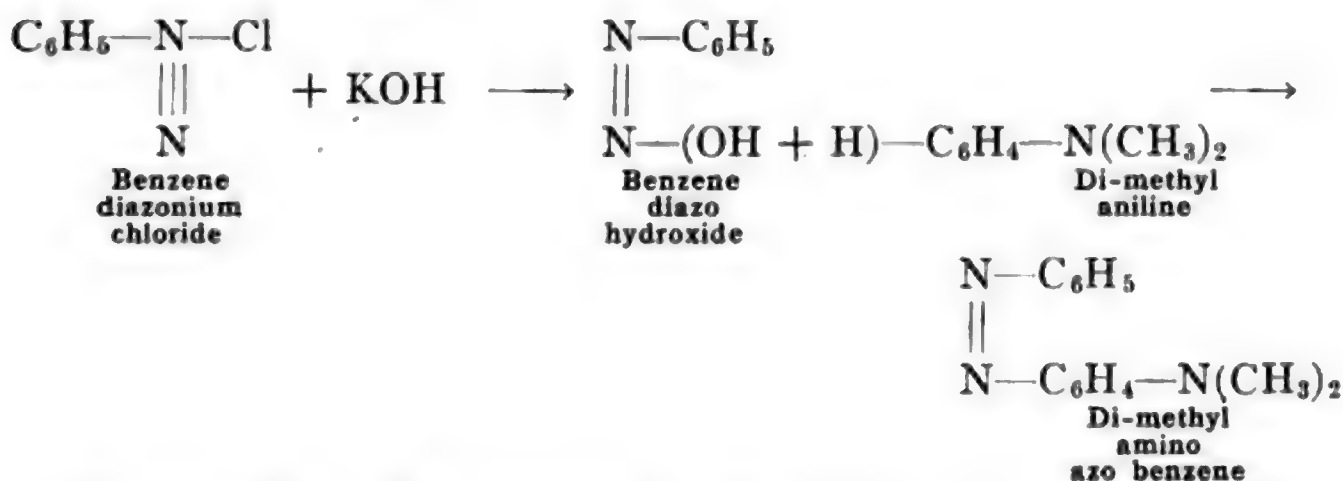
The *syn* form being the more unstable represents the unstable *diazotate*, while the *anti* form is the *iso-diazotate*, the stable compound.

Phenyl Nitroso Amine.—The iso-diazotate differs in a noticeable way from the diazotate. Not only is it more stable, but on treatment with acids it does not yield diazonium salts, but an entirely different compound, viz., **phenyl nitroso amine**, $\text{C}_6\text{H}_5-\text{NH}-\text{NO}$. This compound has the same composition as the **diazo hydroxide** and the relationship means that the isomeric diazo hydroxide undergoes structural rearrangement into a new compound. This is the reason for the view that this same compound, **phenyl nitroso amine**, is an intermediate product in the formation of diazo compounds as already referred to (p. 587). These relationships may be shown as follows:





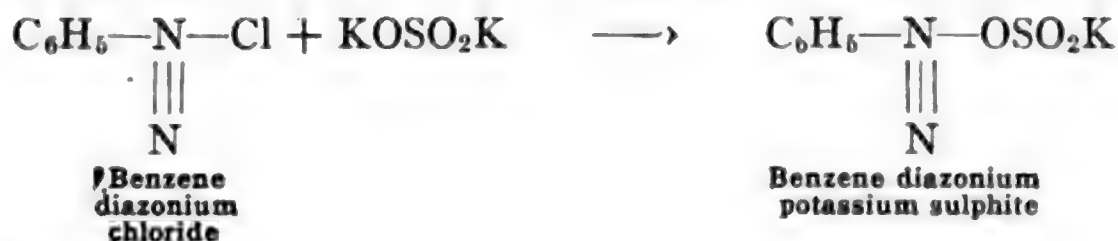
The formation of the diazotate from the diazonium salt by means of alkalis is explained by the reverse of the first reaction. This makes clear the reaction by which the diazonium salts yield azo compounds (p. 569). The reaction takes place best in neutral or alkaline solution and under these conditions the diazonium salt would yield the diazo hydroxide compound which would then couple with the amine and form the amino azo compound.



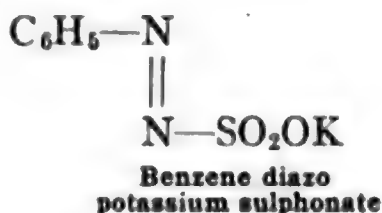
Benzene Diazo Sulphonic Acid.—We should mention here another compound which seems to present a case of isomerism like that of the diazotates. When benzene diazonium chloride is treated in cold alkaline solution with potassium sulphite the following empirical reaction occurs:



This compound is very unstable and explosive and forms hydroxy azo compounds by coupling with hydroxy compounds. Furthermore, it gives sulphur dioxide when treated with dilute acids just as sulphite salts do. It appears, therefore, that this compound is a true diazonium compound, viz., a *diazonium sulphite*, and the reaction should be



Now this unstable compound readily changes in solution into a stable form and this new compound does not act like a sulphite and yield sulphur dioxide with acids, but by reduction it yields the sulphonic acid derivative of phenyl hydrazine. It, therefore is a true *sulphonic acid* derivative of the diazotate form, viz.,

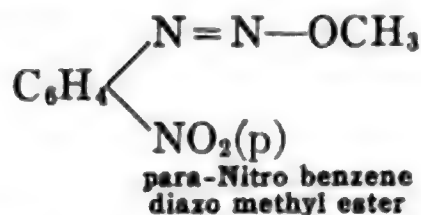


Hantzsch assigns the syn and anti isomeric formulas for the above two compounds but their distinctly different properties, one a sulphite the other a sulphonic acid, seem to indicate that they are tautomeric forms as above, and that the geometric isomer of the sulphonic acid compound is not known.

Thus the acceptance of the **Bloomstrand-Strecker-Erlenmeyer** formula for the diazonium base and salts, and of the **Hantzsch** modification of the **Kekulé** formula for the isomeric diazotates and the acid diazo hydroxide, together with the tautomeric transformations which occur, makes possible the explanation of all the facts which we have considered in the preceding discussion. These may be stated again briefly for the sake of emphasis and review. (1) The reaction of *diazotization*, (2) the *diazonium base* and salts, (3) the *diazotates* and acid diazo hydroxide, (4) the *isomerism* of the diazotates, (5) the *diazonium sulphites* and *diazo sulphonic acids*, (6) the relationship of diazo compounds to *nitroso amines*, (7) to *hydrazines*, (8) the *coupling with amino* and *hydroxy* compounds to form *amino azo* and *hydroxy azo* compounds, (9) the reactions of decomposition. Most of these last reactions we have not considered, but will do so presently and we shall find that they all may be likewise satisfactorily explained. The tautomeric constitution of the diazo compounds, therefore, meets every test and is generally accepted.

Diazo Esters.—Before taking up the reactions of decomposition of diazo compounds there is one other class of derivatives which should be mentioned. As an acid compound **benzene diazo hydroxide** yields *esters*, not by the direct action of alcohols, but by the action of *alkyl halides* upon **silver diazotate**. These esters are stable compounds like

the iso-diazotate and are able to be isolated and studied. The methyl ester of **nitro diazo benzene** will be given as an illustration.



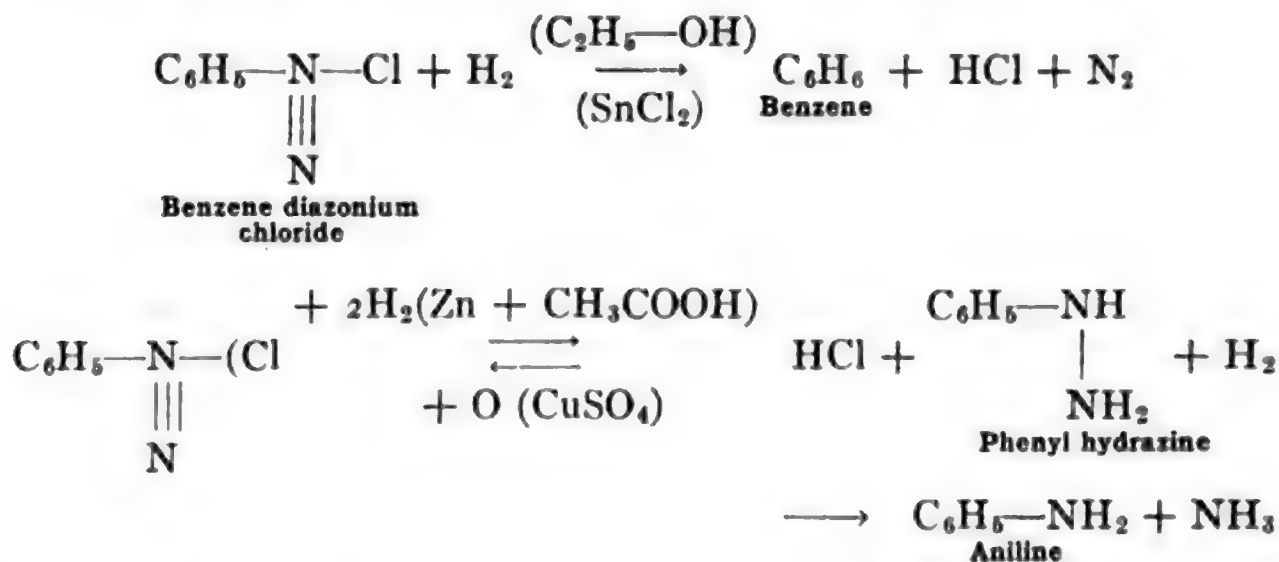
This compound crystallizes in needles which are colorless and which melt at 83° . It is insoluble in water, but soluble in alcohol or ether. Its reactions prove it to be a true diazo compound. It is formed by the action of **methyl iodide** upon either the **silver nitro diazotate** or **iso-diazotate**.

Reactions of Di-azo Compounds

The reactions of diazo compounds are of two types. (1) Reactions by which the nitrogen group is left *intact*. In these the nitrogen group may be *unchanged* in character, the products being *derivatives of diazo compounds*, e.g., *diazonium salts*, *diazotates*, *diazonium sulphites*, *diazosulphonic acids*; or the nitrogen group may be *changed* in character yielding other classes of compounds, e.g., rearrangement to isomeric *nitroso amines*, reduction to *hydrazines*, or coupling to form *azo amino*, *amino azo* or *hydroxy azo* compounds. All of the reactions of this type have been fully considered in the discussion of the constitution of diazo compounds, and in the previous study of azo compounds. (2) Reactions of decomposition in which the diazo nitrogen group is either partly or wholly replaced. The reactions of this second type we shall now consider. We shall use **benzene diazonium chloride** as the example, but it should be emphasized that the reactions are *typical of any diazo compound*. Detailed directions or the particular conditions under which a specific reaction takes place will not be given, but may be found in larger texts or laboratory guides.

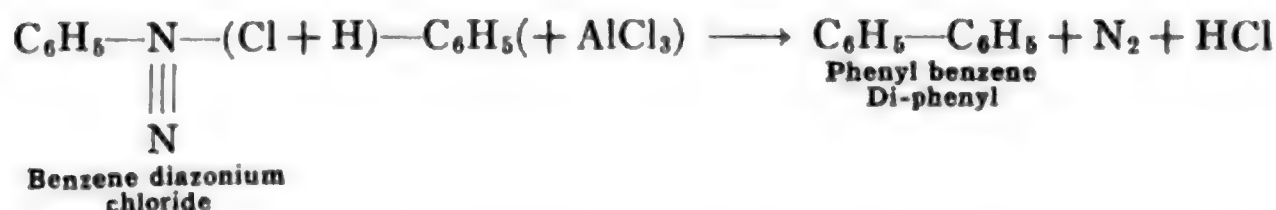
Reduction to Hydrocarbons.—By reducing agents diazo compounds yield the corresponding *hydrocarbon*, the diazo group being replaced by hydrogen. We have already stated (p. 587) that by reduction diazo compounds yield hydrazines in which case the diazo group remains intact though changed in character. This is evidently a further step in the complete reduction which finally results in the hydrazine being split into **aniline** and **ammonia** for the hydrazine may also be trans-

formed back to the diazo compound by oxidation with copper sulphate or ferric chloride. The following reactions will illustrate.

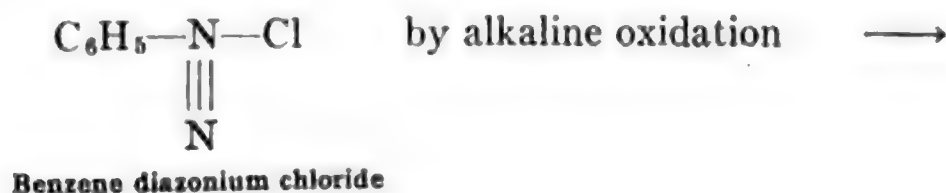


The reduction of diazo compounds to the hydrocarbon may be accomplished by means of **stannous chloride**, **sodium stannite** or under certain conditions *alcohols* act as a reducing agent being themselves thereby oxidized to aldehydes.

Hydrocarbons of another class than the one corresponding to the diazo compound may be obtained by the reaction of diazo compounds with a hydrocarbon in the presence of aluminium chloride (**Friedel-Craft** reaction). In this case the diazo group is replaced by a hydrocarbon radical.



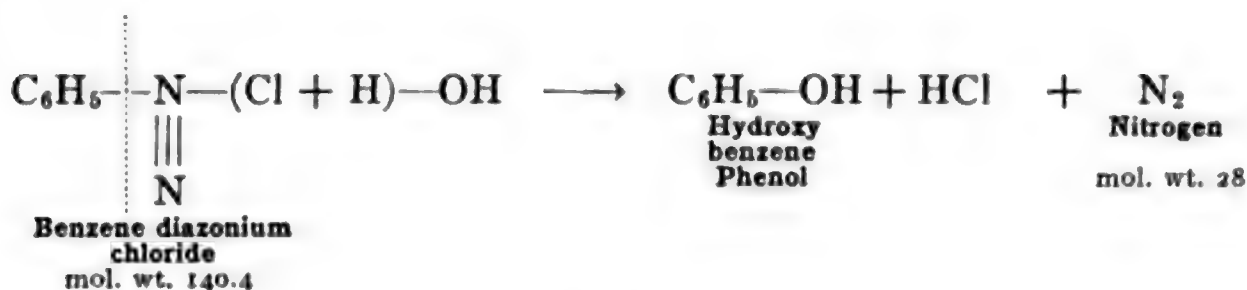
Oxidation.—When oxidized in alkaline solution diazo compounds are converted into a number of different products, in some cases with the loss of nitrogen and in some without. In alkaline permanganate or ferricyanide solutions benzene diazonium salts yield a mixture as follows:



$\text{C}_6\text{H}_5-\text{C}_6\text{H}_5$	Di-phenyl
$\text{C}_6\text{H}_5-\text{N}=\text{N}-\text{C}_6\text{H}_5$	Azo benzene
$\text{C}_6\text{H}_5-\text{NH}(\text{NO}_2)$	Phenyl nitro amine
$\text{C}_6\text{H}_5-\text{NO}$	Nitroso benzene
$\text{C}_6\text{H}_5-\text{NO}_2$	Nitro benzene

As the oxidation occurs in alkaline solution the diazonium salt is first converted into the diazo hydroxide or the diazotate and this is then oxidized.

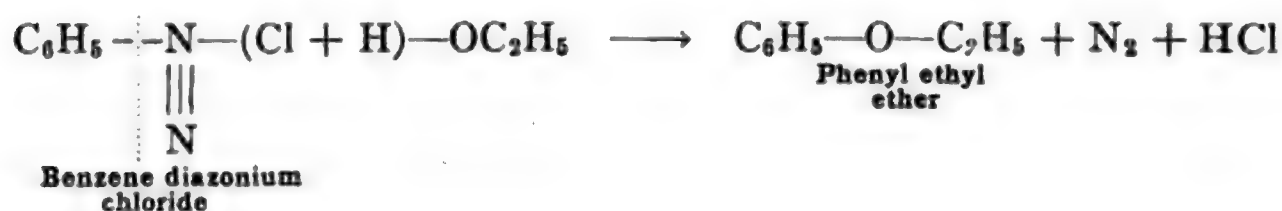
Reaction with Water Yields Phenols.—With water at ordinary or at raised temperatures diazonium salts readily decompose, the nitrogen is set free and the *hydroxyl compound* of the corresponding hydrocarbon is formed, *i.e.*, the diazo group is entirely replaced by the *hydroxyl group*. **Benzene diazonium chloride** thus yields **hydroxy benzene** or **phenol**.



We have referred to this reaction as being the second step in the action of nitrous acid on primary amines as it takes place in the aliphatic series (p. 60). This explains why, in most cases, it is necessary to keep the temperature *low*, usually at about 0° , during diazotization for, if the temperature rises, the reaction just given takes place, which, with the reaction of diazotization, makes the whole double reaction exactly the same as in the case of aliphatic amines. The nitrogen set free is the entire amount present in the diazo compound, and by conducting the operation so as to measure the evolved nitrogen gas, the reaction may be used for a quantitative determination of the amount or purity of the diazo compound, 28 parts by weight of nitrogen (1 mol.) being evolved from 140.4 parts by weight of benzene diazonium chloride.

Alcohols Yield Ethers.—With alkalies a similar reaction does not occur, the more stable diazotates being formed (p. 591). When heated with alcohols, however, the diazo compounds act in an exactly analogous way to that with water. In this case if an aliphatic alcohol

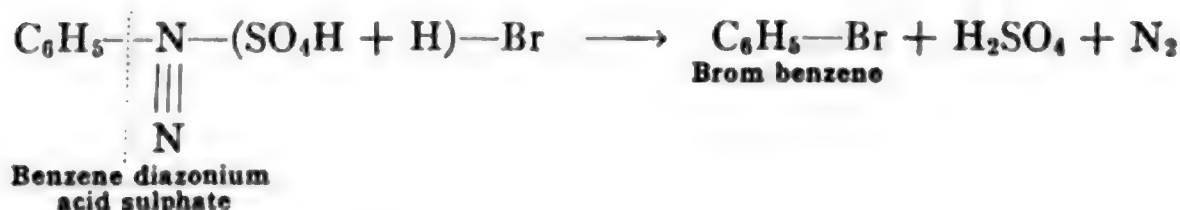
is used the *alkyl oxy* group replaces the diazo nitrogen group and an ether results.



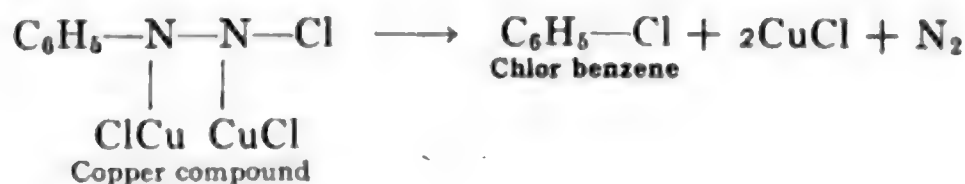
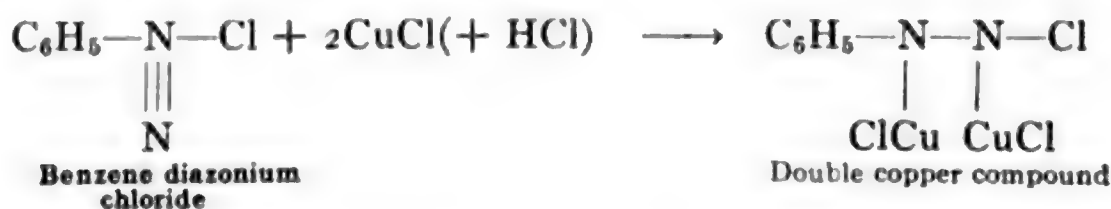
Under certain conditions aromatic ring hydroxy compounds yield analogous products though the usual reaction is the one already given (p. 569) by which hydroxy azo compounds are formed.

Sulphur Compounds.—The two preceding reactions with water and with alcohol may be carried out also with the analogous sulphur compounds, viz., **hydrogen sulphide**, $\text{H}-\text{SH}$, and **thio-alcohols** or **mercaptans**, e.g., $\text{C}_2\text{H}_5-\text{SH}$. The product in the first case is a **thio-phenol**, $\text{C}_6\text{H}_5-\text{SH}$, and in the second **phenyl ethyl thio-ether**, $\text{C}_6\text{H}_5-\text{S}-\text{C}_2\text{H}_5$.

Halogen Acids Yield Aromatic Halides.—When a water solution of a diazonium salt is heated with a halogen acid the halogen substitution product of the corresponding hydrocarbon is obtained, the diazo group being replaced by the halogen.

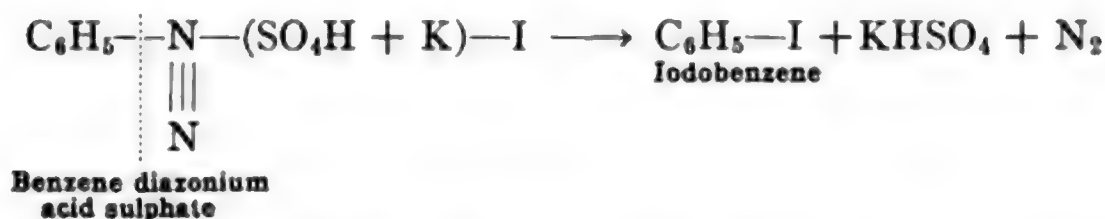


Sandmeyer Reaction.—It was found that in the presence of the cuprous salt of the halogen acid, CuCl or CuBr , the decomposition takes place more easily, a double copper compound being probably formed as an intermediate step.

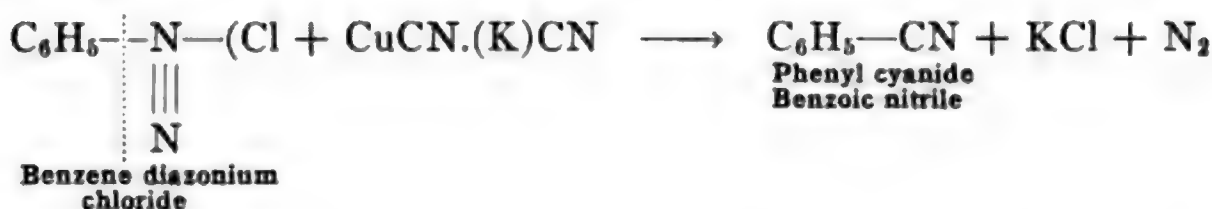


This is known as the **Sandmeyer reaction** and it is usually carried out at the same time as the diazotization so that by starting with the primary amine the halogen product is obtained.

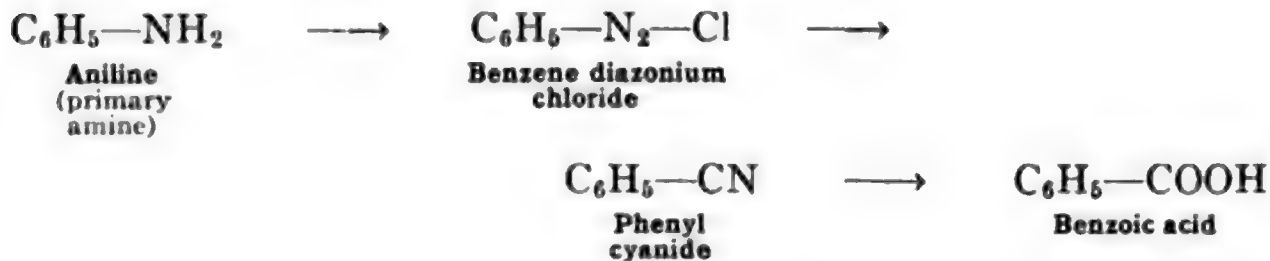
Gattermann Reaction.—The reaction was further modified by **Gattermann** who found that finely divided metallic copper could be used with even greater advantage. The **Sandmeyer** and **Gattermann** reactions are not applicable, however, for the formation of the iodine products. To form these the diazonium salt, usually the acid sulphate, is heated with a solution of potassium iodide.



Cyanides Yield Nitriles.—Sandmeyer also applied the principle of his reaction to the preparation of cyanide substitution products, *i.e.*, replacement of the diazo group with cyanogen radical. The reaction is brought about by warming a diazonium salt solution with a solution of cuprous cyanide in potassium cyanide.



Aromatic Acids.—As the cyanides are *acid nitriles*, yielding the acids on hydrolysis, the above reaction gives us a means of passing from primary amines through the diazo compound to the acid nitrile and finally to the corresponding aromatic acid.



The following tabular arrangement of all of the diazo reactions will bring the whole matter in review.

TABLE XIX.—REACTIONS OF DIAZO COMPOUNDS

Character of reaction	Compound acted upon		Reagent formula	Product formed		Character of product
	Name	Formula		Formula	Name	
Diazotization.....	Aniline hydrochloride.	$\text{C}_6\text{H}_5\text{—N—Cl}$ (H ₂)	O) = N—(OH	$\text{C}_6\text{H}_5\text{—N—Cl}$ N	Benzene diazonium chloride.	Neutral salt.
Metathesis.....	Benzene diazonium chloride.	$\text{C}_6\text{H}_5\text{—N—(Cl)}$ N	Ag)—OH	$\text{C}_6\text{H}_5\text{—N—OH}$ N	Benzene diazonium hydroxide.	Base (not isolated).
Ditto, with structural rearrangement.	Ditto.....	$\text{C}_6\text{H}_5\text{—N—(Cl)}$ N	K)—OH	$\text{C}_6\text{H}_5\text{—N—N}$ HO—N	Benzene diazo hydroxide.	Acid (not isolated).
Neutralization....	Benzene diazo hydroxide	$\text{C}_6\text{H}_5\text{—N—N}$ HO—N	K—OH	$\text{C}_6\text{H}_5\text{—N—N}$ KO—N	Potassium benzene diazotate.	Alkali salt, unstable.
Stereo rearrangement.	Potassium benzene diazotate.	$\text{C}_6\text{H}_5\text{—N—N}$ KO—N	Heat and strong alkaline sol.	$\text{C}_6\text{H}_5\text{—N—N}$ N—OK	Potassium benzene isodiazotate.	Isomeric alkali salt, stable.
Metathesis.....	Benzene diazonium chloride.	$\text{C}_6\text{H}_5\text{—N—(Cl)}$ N	K)O—SO ₂ K	$\text{C}_6\text{H}_5\text{—N—O—SO}_2\text{K}$ N	Potassium benzene diazonium sulphite.	Neutral salt.
Structural rearrangement.	Potassium benzene diazonium sulphite.	$\text{C}_6\text{H}_5\text{—N—OSO}_2\text{K}$ N	→	$\text{C}_6\text{H}_5\text{—N—N}$ N—SO ₂ —OK	Benzene diazo sulphonate.	Sulphonic acid salt.
Metathesis with structural rearrangement.	Potassium benzene isodiazotate.	$\text{C}_6\text{H}_5\text{—N—N}$ N—O(K	Cl)H	$\text{C}_6\text{H}_5\text{—NH—NO}$	Phenyl nitroso amine.	Nitroso amine.

Esterification.....	Silver benzene iso- diazotate. Benzene diazonium chloride.	$\text{C}_6\text{H}_5-\text{N} \begin{array}{c} \parallel \\ \text{N}-\text{O}(\text{Ag}) \\ \text{C}_6\text{H}_5-\text{N}-\text{N}-(\text{Cl}) \\ \parallel \\ \text{N} \end{array}$	$\text{C}_6\text{H}_5-\text{N} \begin{array}{c} \parallel \\ \text{N}-\text{OCH}_3 \\ \text{C}_6\text{H}_5-\text{N} = \text{N}-\text{NH}-\text{C}_6\text{H}_5 \end{array}$	$\text{C}_6\text{H}_5-\text{N} \begin{array}{c} \parallel \\ \text{N}-\text{OCH}_3 \\ \text{C}_6\text{H}_5-\text{N} = \text{N}-\text{NH}-\text{C}_6\text{H}_5 \end{array}$	Methyl benzene iso- diazotate. Diaz amino benzene.	Ester.
Replacement and rearrangement without loss of nitrogen. (Griess reaction.)			(Neutral or weakly acid solution.)			Diazo amino compound.
Structural rear- rangement.	Diazo amino benzene.	$\text{C}_6\text{H}_5-\text{N} = \text{N}-\text{NH}-\text{C}_6\text{H}_5$	→	$\text{C}_6\text{H}_5-\text{N} = \text{N}-\text{C}_6\text{H}_5-\text{NH}_2$	Amino azo benzene.	Amino azo compound.
Replacement and rearrangement without loss of nitrogen. (Griess reaction.)	Benzene diazonium chloride.	$\text{C}_6\text{H}_5-\text{N}-(\text{Cl})$	H)→C ₆ H ₅ -N(CH ₃);	$\text{C}_6\text{H}_5-\text{N} = \text{N}-\text{C}_6\text{H}_5-\text{N}(\text{CH}_3)_2$	Di-methyl amino azo benzene.	Amino azo compound.
Ditto.....	Ditto.....	$\text{C}_6\text{H}_5-\text{N}-(\text{Cl})$	H)→C ₆ H ₅ -OH	$\text{C}_6\text{H}_5-\text{N} = \text{N}-\text{C}_6\text{H}_5-\text{OH}$	Hydroxy azo benzene.	Hydroxy azo compound.
Oxidation.....	Ditto.....	$\text{C}_6\text{H}_5-\text{N}-\text{Cl}$	O; (alkaline KMnO ₄)	$\text{C}_6\text{H}_5-\text{NH}(\text{NO}_2)$	Phenyl nitro amine.	Nitro amine.
				$\text{C}_6\text{H}_5-\text{N} = \text{N}-\text{C}_6\text{H}_5$	Azo benzene.	Azo com- pound.
				$\text{C}_6\text{H}_5-\text{NO}$	Nitroso benzene.	Nitroso compound.
				$\text{C}_6\text{H}_5-\text{NO}_2$	Nitro benzene.	Nitro compound.
				$\text{C}_6\text{H}_5-\text{C}_6\text{H}_5$	Di-phenyl.	Hydrocarbon.
Reduction without loss of nitrogen.	Ditto.....	$\text{C}_6\text{H}_5-\text{N}-\text{Cl}$	H; (Zn + CH ₃ -COOH)	$\text{C}_6\text{H}_5-\text{NH}-\text{NH}_2$	Phenyl hydrazine.	Hydrazine.

TABLE XIX.—REACTIONS OF DIAZO COMPOUNDS (Continued)

Character of reaction	Compound acted upon		Reagent formula	Product formed		Character of product
	Name	Formula		Formula	Name	
Reduction with loss of nitrogen. Replacement of diazo group with H .	Benzene diazonium chloride.	$C_6H_5-N \equiv N-Cl$	$H-H$ (C_6H_5-OH or $SnCl_2$)	C_6H_6	<i>Benzene.</i>	Hydrocarbon.
Replacement of diazo group with C_6H_5 .	Ditto.....	$C_6H_5-N \equiv N-Cl$	$H-C_6H_5$ (+ $AlCl_3$)	$C_6H_5-C_6H_5$	<i>Di-phenyl.</i>	Hydrocarbon.
Ditto, with OH	Ditto.....	$C_6H_5-N \equiv N-Cl$	$H-OH$	C_6H_5-OH	<i>Phenol.</i>	Phenol.
Ditto, with OR	Ditto.....	$C_6H_5-N \equiv N-Cl$	$H-O-C_6H_5$	$C_6H_5-O-C_6H_5$	<i>Phenyl ethyl ether.</i>	Ether.
Ditto, with SH	Ditto.....	$C_6H_5-N \equiv N-Cl$	$H-SH$	C_6H_5-SH	<i>Thio-phenol.</i>	Thio-phenol.
Ditto, with SR	Ditto.....	$C_6H_5-N \equiv N-Cl$	$H-S-C_6H_5$	$C_6H_5-S-C_6H_5$	<i>Phenyl ethyl thio-ether.</i>	Thio-ether.

Ditto with $Br(Cl)$.	Benzene diazonium sulphate.	$C_6H_5-\overset{ }{N}-N-(SO_3H)$	$H)-Br$	C_6H_5-Br	<i>Brom benzene.</i>	Aryl halide.
Ditto, with I	Ditto.....	$C_6H_5-\overset{ }{N}-N-(SO_3H)$	$K)-I$	C_6H_5-I	<i>Iodo benzene.</i>	Ditto.
Ditto, with $Cl(Br)$ (Sandmeyer).	Benzene diazonium chloride.	$C_6H_5-\overset{ }{N}-N-(Cl)$	$H)-Cl + CuCl$	C_6H_5-Cl	<i>Chlor benzene.</i>	Ditto.
Ditto (Gattermann).	Ditto.....	$C_6H_5-\overset{ }{N}-N-(Cl)$	$H)-Cl + Cu$	C_6H_5-Cl	<i>Chlor benzene.</i>	Ditto.
Ditto, with CN	Ditto..	$C_6H_5-\overset{ }{N}-N-(Cl)$	$K)-CN.CuCN$	C_6H_5-CN $\downarrow + H_2O$ C_6H_5-COOH	Phenyl cyanide. Benzoic nitrile. Benzoic acid.	Acid nitrile. Acid.

Looking at these reactions as a whole we can not fail to recognize how extremely reactive the diazo compounds are, and what varied products result. The instability which we find here as in other organic nitrogen compounds, while not of practical application in explosives, gives to the compounds their exceeding ease of reaction. As they are themselves prepared from primary amines of the aromatic series, and as the amines are either natural products obtained from coal tar or are easily prepared from the hydrocarbons, through the like easily prepared nitro compounds, the chemist has, in the diazo compounds, a practical means of obtaining a large variety of products. These products may have a direct value as dyes, as in the case of many of the different groups of azo compounds, or they may be steps in the preparation of other compounds, as is true of most of the decomposition products obtained by replacing the diazo group with *hydrogen, hydroxyl, a halogen, cyanogen*, etc. As the formation of diazo compounds takes place with any primary amine, whether a simple compound or a complex substitution product, and whether of benzene or its homologues, or of the other series of hydrocarbons, the last reactions just referred to are used as a means of obtaining practically any derivative of the classes given. Thus both industrially and theoretically the diazo compounds are of great practical use, not in themselves as isolated compounds, but as steps in the preparation of other products.

RESUMÉ OF NITROGEN DERIVATIVES

In the last four main groups of benzene derivatives, viz., the *nitric* and *nitrous acid derivatives*, the *ammonia derivatives* or *amines*, the *intermediate reduction products of nitro compounds*, and the *diazo compounds*, we have to do with organic compounds containing **nitrogen**. These four groups do not include all of the organic nitrogen compounds of the aromatic series, as the large and important group of basic nitrogen compounds including the alkaloids will be studied later. Even with this exception the four groups considered show us how important the aromatic nitrogen compounds are. The presence of nitrogen in the molecule endows the compounds with many characteristic properties such as *instability*, resulting in extreme *reactivity* and often connected with *explosive* character. The compounds also often exhibit the phenomena of *isomerism* both *structural* and *stereo-*, and of *tautomerism*.

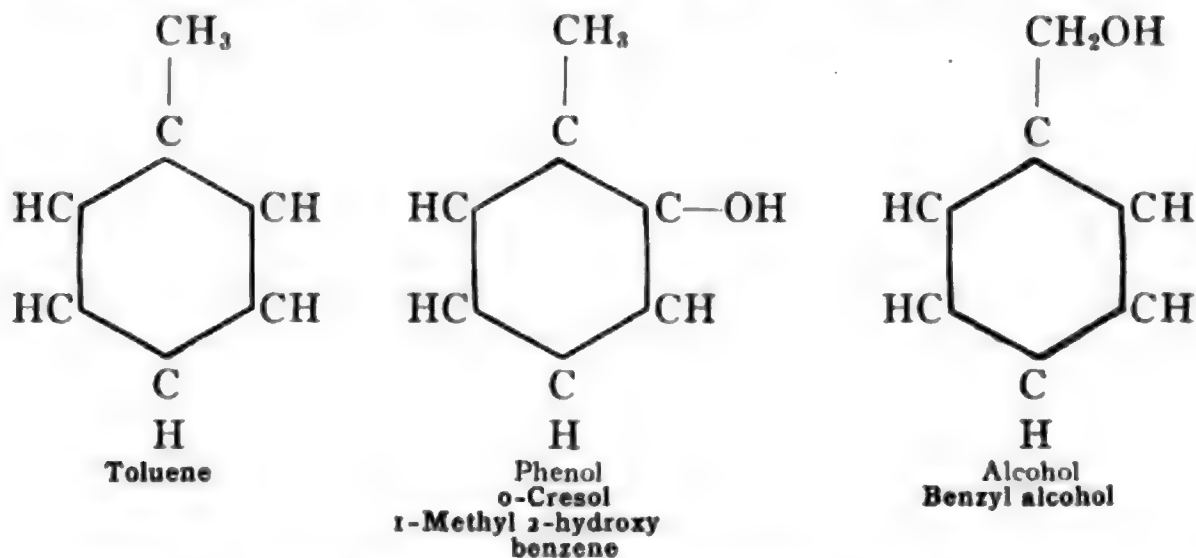
Practical application of the explosive character of nitrogen compounds is found in the case of the nitro compounds such as **tri-nitro toluene** and nitro phenols such as **picric acid** (p. 630) which are analogous as nitro compounds to similar explosives of the aliphatic series, *e.g.*, **nitro glycerol** and **nitro cellulose**. The chemical reactivity of the nitrogen compounds as shown in their ability to yield a large variety of products is found in the groups of *amines*, the *intermediate reduction products* of nitro compounds and above all in the *diazo compounds*. All of these groups are associated in their relation to the numerous important products used as dyes, in particular those of the azo and benzidine classes, while the amines themselves are related to other like important dyes such as the **tri-phenyl methane** and **indigo** classes. Thus as a large class the aromatic nitrogen compounds are almost without a parallel as to their importance both from an industrial or economic and from a theoretical viewpoint.

VII. HYDROXYL DERIVATIVES

A. PHENOLS

(*Hydroxyl in the ring*)

We come now to the hydroxyl substitution products of the benzene hydrocarbons. These derivatives are of two classes: *A*, *phenols*, in which the hydroxyl group is substituted in the ring part of the compound. *B*, *alcohols*, in which the hydroxyl group is substituted in the side chain of benzene homologues. Benzene having no side chain yields only the first class of derivatives. Toluene, however, and all the other homologues of benzene yield both classes as follows:



Phenols.—The ring hydroxyl compounds take the class name of *phenols* from the simplest member, *hydroxy benzene* or **phenol**. These are true aromatic compounds and in methods of formation, reactions and properties are distinctly different from aliphatic hydroxyl compounds or alcohols. Their outstanding distinction is their marked *acid* character, the alcohols being *neutral* (p. 103). This is attributed to the influence of the *phenyl* radical (C_6H_5-). The same influence is present in the amino derivatives, for the ring amines, $\text{C}_6\text{H}_5-\text{NH}_2$,

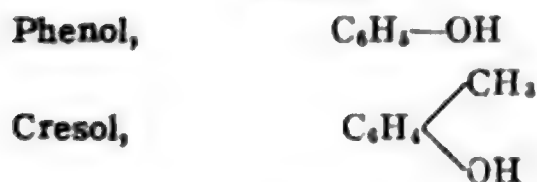
aniline, $\text{C}_6\text{H}_4 \begin{array}{l} \text{CH}_3 \\ \text{NH}_2 \end{array}$, **toluidine**, etc., are *less basic*, i.e., more acid, than aliphatic amines, e.g., CH_3-NH_2 , methyl amine, and also than $\text{C}_6\text{H}_5-\text{NH}(\text{CH}_3)$, **mono-methyl aniline**, or $\text{C}_6\text{H}_5-\text{N}(\text{CH}_3)_2$, **di-methyl aniline**.

Alcohols.—The side chain hydroxyl compounds take the class name of alcohols for they are true aromatic alcohols in formation, reaction and properties. They are *neutral*, not acid, and are formed by methods analogous to those by which the aliphatic alcohols are prepared. They may be looked upon as benzene derivatives of aliphatic alcohols, *e.g.*, $C_6H_5-CH_2OH$, **benzyl alcohol** or phenyl methyl alcohol.

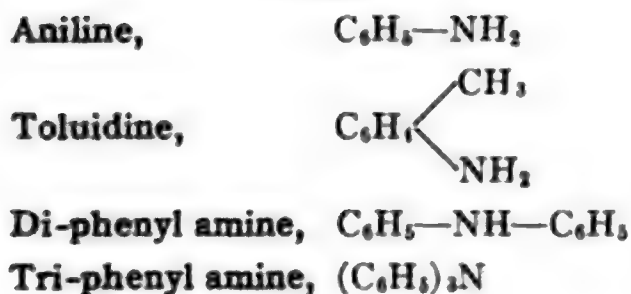
The acidic influence of the benzene ring or phenyl radical may be illustrated by a comparison of the two series of compounds given below.

AROMATIC CHARACTER
ring substitution
(more acid; less basic)

Phenols

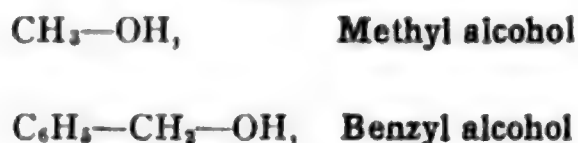


Amines

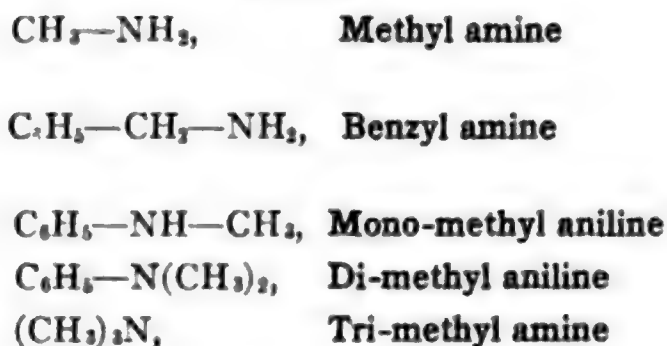


ALIPHATIC CHARACTER
chain substitution
(more basic; less acid)

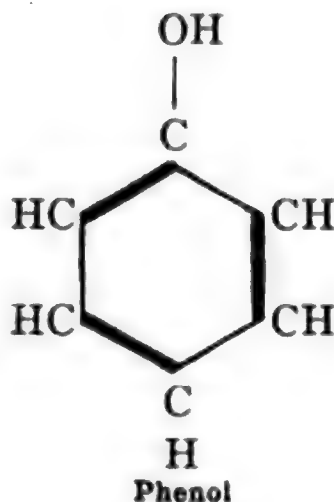
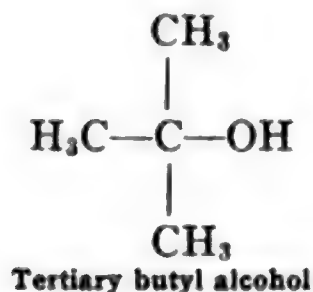
Alcohols



Amines



If we examine the complete benzene ring formulas for the phenols we see that the carbon-hydroxyl group is of the same nature as in *tertiary* alcohols.



In both cases the carbon atom linked to the hydroxyl has the three other valencies satisfied by carbon groups. In the tertiary alcohols three separate carbon groups satisfy the three valencies while in the phenol only two carbon groups satisfy the three valencies, one of them being doubly linked. The phenols thus are not even in this respect exactly like the alcohols, and though they do resemble the tertiary alcohols in not yielding either aldehydes or ketones on oxidation, due to the fact that no hydrogen atom is linked to the hydroxyl carbon atom, yet the fact that they are distinctly different from the alcohols should always be kept in mind.

Mono- and Poly-phenols.—As with the other ring substitution products of benzene and its homologues we have not only *mono-*, but also *di-*, *tri-* and other poly-substitution products, so also we have poly-phenols in which more than one hydrogen atom of the ring is substituted by the hydroxyl group. In these poly phenols the conditions of position isomerism are present so that *ortho*, *meta* and *para*; *vicinal*, *symmetrical* and *unsymmetrical* isomers are known.

Syntheses

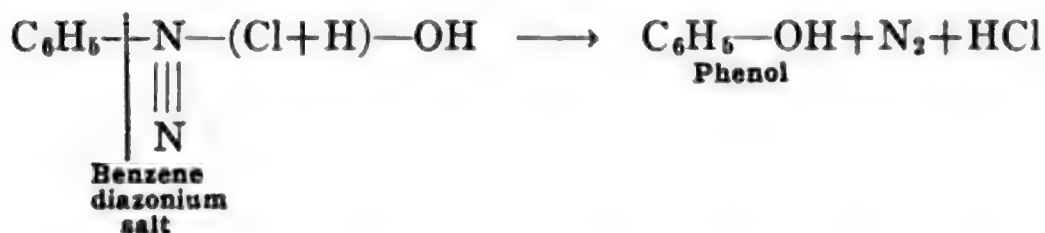
From Sulphonic Acids.—As previously stated, the methods of formation of phenols are wholly different from those of alcohols, and, together with their reactions, prove the constitution to be as we have given it, viz., *Ring—OH*. The synthesis which is most generally used industrially is that from *sulphonic acids*, (p. 520). When a salt of *benzene sulphonic acid* is fused with potassium or sodium hydroxide, **phenol** is formed together with a *sulphite* salt of the metal, according to the following reaction:



The phenol is present in the fusion product as the potassium salt formed by neutralization of the acid phenol with the excess of alkali. On acidifying the phenol separates and at the same time sulphur dioxide is evolved proving that a salt of sulphurous acid is present. The relation of this reaction to the sulphonic acids and to sulphurous acid has been discussed in connection with the sulphonic acids (p. 520).

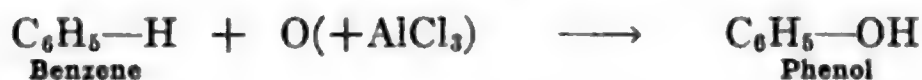
From Diazo Compounds.—Another synthesis of phenols that is often used in the laboratory, especially if the desired sulphonic acid is not

known or is unavailable, is the one from *diazo compounds* which has already been given in connection with the reactions of these compounds (p. 597). When decomposed by water *diazonium salts* have the diazo group replaced by hydroxyl.



This synthesis gives a method of preparing phenols from amino derivatives by first diazotizing these and then decomposing the diazo compound as above. Also nitro derivatives may be reduced to amines and then converted into phenols. Thus from either of these classes of compounds by means of the diazo reactions we may obtain the corresponding phenol with the hydroxyl group in the position of the original nitro or amino group. Such a result is often desired in synthetic work and the diazo synthesis of phenols is of great importance.

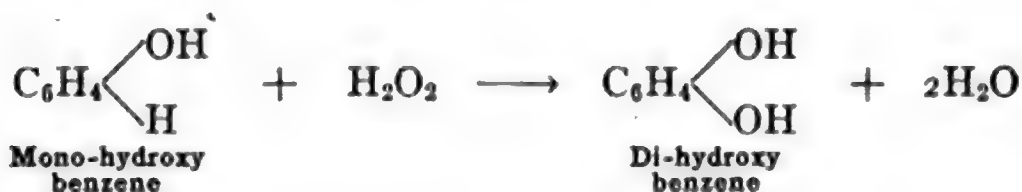
From Hydrocarbons.—In the presence of aluminium chloride (Friedel-Craft reagent) benzene may be oxidized to phenol.



It will be recalled that aliphatic hydrocarbons containing a tertiary carbon group,



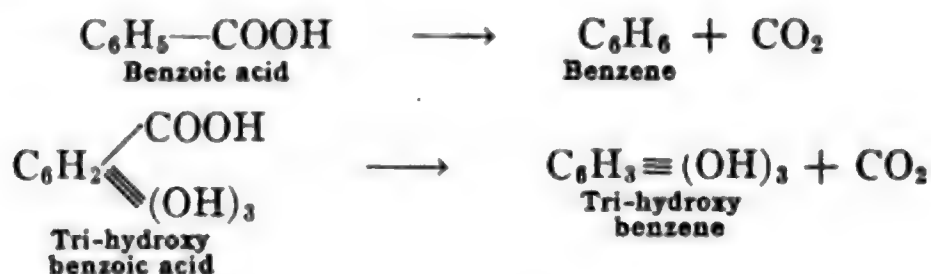
are easily oxidized to tertiary alcohols (p. 239). This emphasizes the tertiary alcohol similarity of the phenols before referred to. In the case of *di-phenols* it is a striking fact that they may be prepared by oxidizing a mono-phenol by means of **hydrogen dioxide**.



Reactions of this kind do not occur in the aliphatic series.

From Hydroxy Acids.—Carboxylic acids when heated with soda lime lose carbon dioxide and yield the hydrocarbon. By a similar reaction hydroxy acids, either aliphatic or aromatic, which contain a

hydroxyl group as well as a carboxyl, yield the hydroxyl derivative of the hydrocarbon.



The reaction is not practical for the preparation of phenol itself, but is used in the case of the *tri-hydroxy benzene*, **pyro-gallol** or **pyro-gallic acid** which is obtained by heating **gallic acid**, which is *tri-hydroxy benzoic acid*, as above.

From Aryl Halides.—We have said that phenols are not prepared by the same general reactions as are used in preparing the aliphatic hydroxyl compounds. This is true in general though we shall give an interesting exception. Aliphatic alcohols are most easily synthesized by treating the *alkyl halides* with silver hydroxide, or with potassium hydroxide.



With the simple aryl halides such as the mono-chlor derivatives of benzene or its homologues this reaction does not take place. If, however, a benzene halide has also substituted in the ring two nitro, sulphonic acid or carboxyl groups, in the ortho and para positions to the halogen, then treatment of the halide with potassium hydroxide results in replacing the halogen with hydroxyl and the corresponding substituted phenol will be obtained.

From Natural Sources.—In addition to their synthetic preparation many of the phenols are obtained by the distillation of natural substances, *e.g.*, coal (coal tar), wood, resins, etc. Phenol is obtained from coal tar, while the **hydroxy toluenes** or **cresols** are obtained from both wood tar and coal tar as indicated by the term *creosote* for the crude distillation products of wood.

Properties and Reactions

The mono-phenols are liquids or low melting-point crystalline solids, while the poly-phenols are crystalline solids only. The mono-phenols

are soluble in alcohol or ether but only slightly so in water. As the number of hydroxyl groups increases, the solubility in water also increases, the *di-* and *tri-hydroxyl* derivatives being easily soluble in water.

Salts.—As has been stated, the acid nature of the phenols is a distinctive character. This is especially true of the lower members, **phenol**, the simplest member, being commonly known as **carbolic acid**. In the case of certain substituted phenols the acid character is even more marked, *e.g.*, **picric acid**, which is **tri-nitro phenol**. As acids the phenols readily form salts termed phenolates.

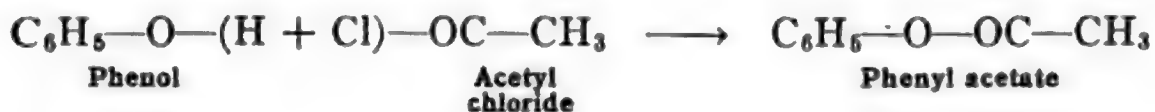


While alcohols also form *alcoholates* (p. 79), the *phenolates* are more stable and more definitely salt-like in character due to the more strongly acid nature of the *phenyl* or other *aryl* radical. The phenolates, however, are decomposed by carbon dioxide and react alkaline to some indicators.

Esters.—While not true alcohols, the phenols nevertheless possess alcoholic character as already referred to in speaking of their similarity to tertiary alcohols. This is shown in their formation of both *esters* and *ethers*. Esterification is as a rule less easy than with alcohols. Phenolates absorb carbon dioxide directly yielding a compound that is a mixed ester and salt of carbonic acid.



This compound will be referred to again in connection with the synthesis of **salicylic acid** (p. 717). The acid ester of phenol and sulphuric acid, **phenyl sulphuric acid**, $\text{C}_6\text{H}_5\text{—O—SO}_2\text{OH}$, is a constituent of animal urine. The esters of phenols and organic acids are not readily formed by the direct action of the acids, in which respect the phenols again resemble tertiary alcohols. They may be prepared from phenols by the action of *acid chlorides*, *acid anhydrides* or a mixture of the *acid* and *phosphorus oxychloride*.

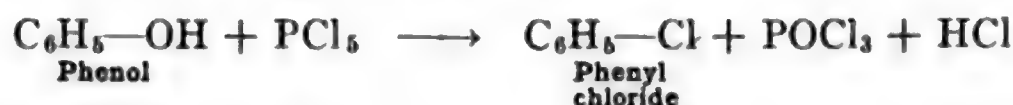


Ethers.—Ethers of the phenols may be formed by means of the **Williamson** reaction when phenolates are treated with alkyl halides.

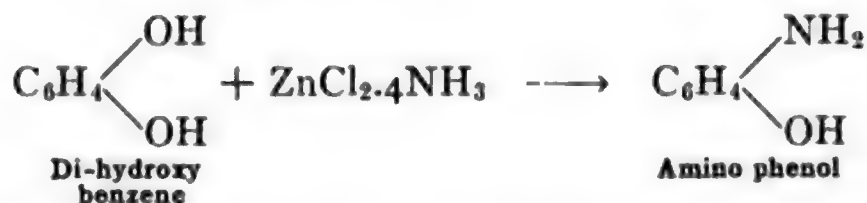


These two ethers, known as **anisole** and **phenetole**, are well known compounds.

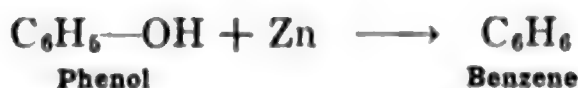
Reaction with PCl_5 .—With phosphorus penta-chloride the phenols react as alcohols yielding the *aryl halide*.



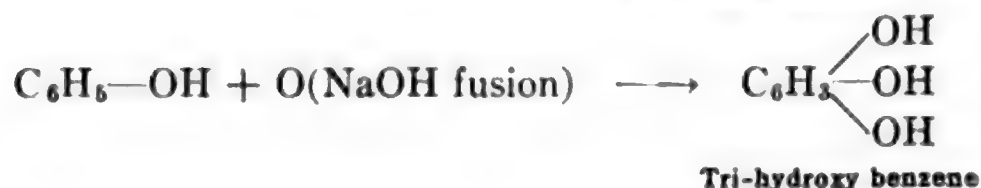
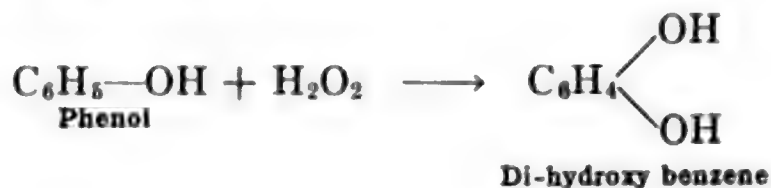
With Ammonia.—With ammonia, in the form of **ammonia zinc chloride**, $\text{ZnCl}_2\text{—}4\text{NH}_3$, phenols, especially the poly-phenols, yield *amino* compounds by replacement of a hydroxyl with an amino group.



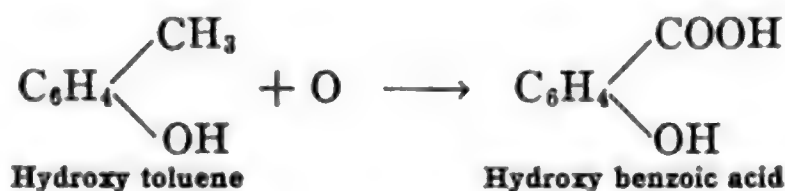
Reduction and Oxidation.—By reduction with zinc, phenols yield hydrocarbons.



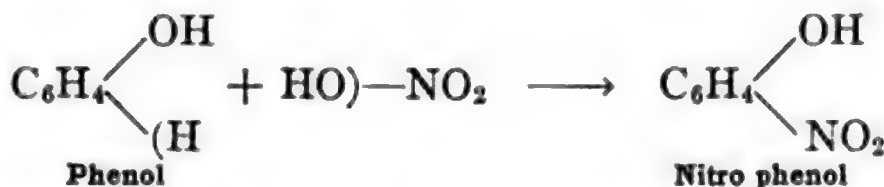
Oxidation of phenols yields a variety of products. Hydrogen dioxide gives a di-hydroxyl product while by fusion with caustic soda both di- and tri-hydroxyl products are obtained.



The phenols of the benzene homologues, *e.g.*, *hydroxy toluenes* or **cresols**, have the side chain group oxidized to carboxyl and yield, therefore, a *hydroxy acid*.



Substitution in the Ring.—With nitric and sulphuric acids phenols yield substitution products more easily than do the hydrocarbons themselves.



Color Reactions.—Many of the derivatives of phenol are highly colored, especially the *nitroso* and *nitro* compounds. The formation of these compounds under qualitative conditions is often made use of in testing either for a phenol or for nitrous or nitric acid or a derivative. With **ferric chloride**, FeCl_3 , phenols give characteristic colors, *blue, green, red* or *violet*. Phenol ethers do not respond to these tests.

Liebermann's Nitroso Reaction.—When phenol in sulphuric acid, **phenyl sulphuric acid**, is treated with a *nitrite* or with a *nitroso amine* a dark green, red or brown color is obtained which changes to blue or green on addition of an alkali. The test is known as **Liebermann's nitroso reaction**, and may be used in testing for a *phenol*, a *nitrite* or a *nitroso amine*.

MONO-PHENOLS, MONO-HYDROXY BENZENES

Phenol, $\text{C}_6\text{H}_5\text{—OH}$, **Hydroxy Benzene**, Carbolic Acid

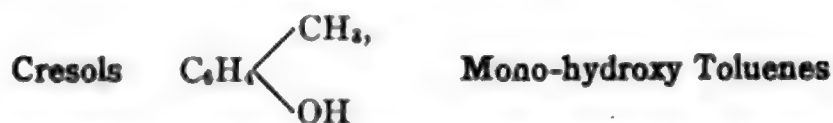
The simplest ring hydroxyl derivative of the benzene hydrocarbons is *mono-hydroxy benzene*, $\text{C}_6\text{H}_5\text{—OH}$. It is known as **phenol** and gives its name to the entire class of ring hydroxy compounds. The name **phenol** is derived from the Greek word *φαινειν*, meaning *to light*, and signifies the occurrence of the substance in the products of illuminating gas manufacture (p. 497). The prefix *phen* is also retained in the term *phenyl* for the benzene radical, $(\text{C}_6\text{H}_5\text{—})$. Phenol is a common pharmaceutical product and is known in pharmacy and medicine as **carbolic acid** indicating its acid properties. This name also signifies

its occurrence in coal tar, being a contraction of *carbon oil acid*. It is one of the five most important products of coal tar distillation in which it was first discovered in 1834 by **Runge**. It also occurs in small amounts in wood tar and in the distillation products of bones. It is present as the sulphuric acid ester, **phenyl sulphuric acid**, $\text{C}_6\text{H}_5\text{—O—SO}_2\text{—OH}$, in animal urine.

Phenol when pure is a colorless crystalline substance with a characteristic odor; m.p. 42.5° , b.p. 181.5° . The presence of a small amount of water lowers the melting point to about 16° , through the formation of a crystalline hydrate, $2\text{C}_6\text{H}_5\text{—OH.H}_2\text{O}$. With more water a solution of water in phenol results which remains liquid. Water is soluble in phenol, 1 : 3, while phenol is soluble in water at ordinary temperatures, 1 : 16.

Poison and Antiseptic.—It is miscible in all proportions with alcohol or ether. Phenol is a very strong poison and is caustic to the skin producing bad burns. As an antidote for phenol poisoning lime or chalk is used. It is an extremely important medicinal substance because of its antiseptic and disinfectant properties, both the hands and instruments of surgeons being rendered aseptic by washing in a dilute, 2 to 3 per cent, solution which is the strength commonly used as an aseptic wash. It has many other important uses, as some of its derivatives, which we shall mention later, are valuable as dyes, explosives and photographic developers. The test for phenol is the one with ferric chloride, as previously given.

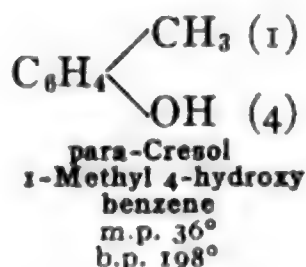
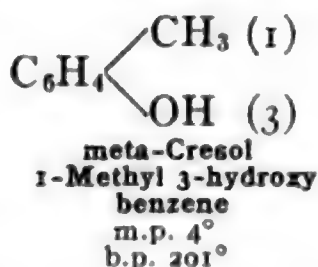
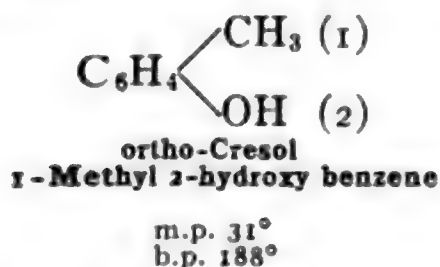
Commercial Preparation.—The most important method for preparing phenol on a commercial scale is the potash fusion of **benzene sulphonate** (p. 520), though it may also be prepared by the diazo synthesis (p. 597). Its chief natural source is coal tar, from which it is obtained in the fractions of coal tar distillation, boiling below 210° , *i.e.*, in the *light* and *middle oils* (p. 497). The process of isolating it has been described (p. 498), the purest product being in the form of the hydrate, m.p. 16° . The yield from coal tar is 0.4 to 0.5 per cent, it being one of the five most important coal tar distillation products.



Mono-hydroxy toluene, being a di-substitution product of benzene, *i.e.*, *methyl hydroxy benzene*, exists in isomeric forms as **ortho**, **meta** and

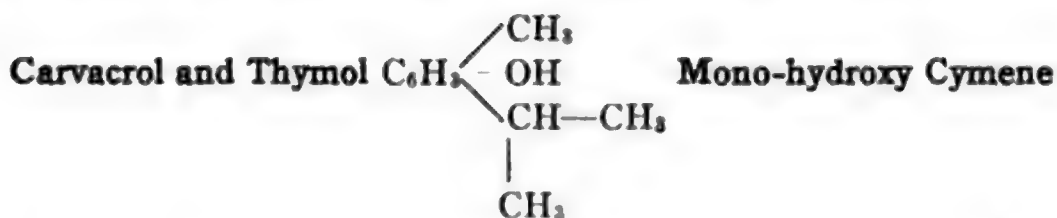
para compounds. They are known as **cresols** and are found in wood tar, and in coal tar in the same fractions of the distillate as phenol. In the higher fractions termed *creosote oils* they are also present, but are not usually separated commercially. The yield of cresols from coal tar is about 2 to 3 per cent.

Tri-cresol.—The product as obtained from coal tar is a mixture of all three isomers and is known as *tri-cresol*. The properties of the cresols are in general like those of phenol. They also are valuable antiseptics being largely used as disinfectants.

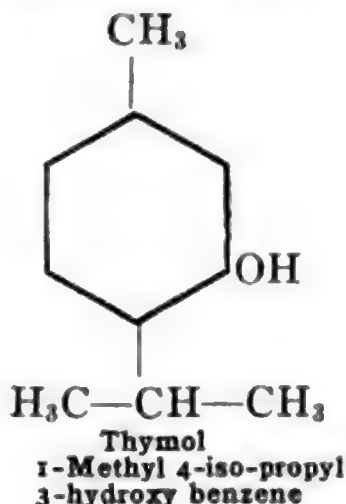
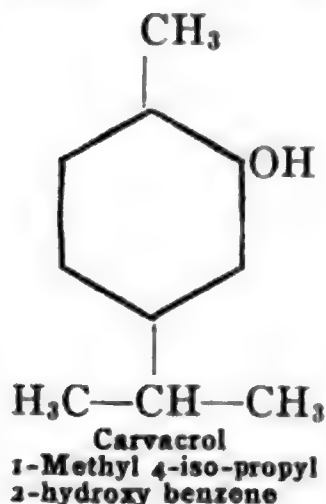


The synthesis of the cresols may be accomplished by the general methods for synthesizing phenols, the meta-cresol being also synthesized from thymol (p. 616). The *ortho*- and *para*-cresols occur as the sulphuric acid esters in human urine, and in larger amounts in the urine of horses.

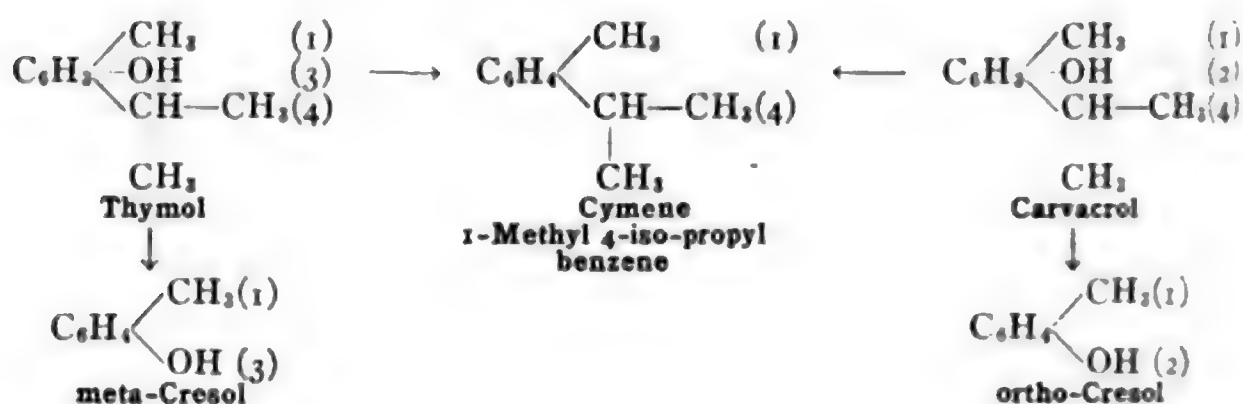
para-Cresol is a product of the putrefaction of proteins.



Only two of the higher homologous mono-hydroxy phenols will be mentioned. These are the two isomeric *mono-hydroxy cymenes*, **cymene** being 1-methyl 4-iso-propyl benzene. They are as follows:



The proofs for the above constitutions are as follows: (1) **Thymol** yields **cymene**, **1-methyl 4-iso-propyl benzene**, by *loss of the hydroxyl oxygen* by means of phosphorus penta-sulphide. (2) **Carvacrol** may be synthesized from **potassium cymene sulphonate** by fusion with potassium hydroxide. Therefore both must be *mono-hydroxy cymenes*. (3) **Thymol** by means of phosphorus pentoxide splits off the iso-propyl radical yielding **meta-cresol** and **propylene**. (4) **Carvacrol** by the same reaction yields **ortho-cresol**. Therefore in **thymol** the hydroxy group is *meta* to the methyl group while in **carvacrol** it is *ortho*. The following relationships are thus established.



Terpenes and Camphor.—The importance of these two phenols is in their natural occurrence as ethers in *ethereal oils* of many plants, *e.g.* *oil of thyme* and *oil of caraway*, and especially in their relationship to the **terpenes** and **camphor**, as will be shown later (p. 826, 834).

Phenols derived from benzene homologues containing an *unsaturated* side chain will be mentioned later in discussing *ether* derivatives of phenols (p. 622).

POLY-PHENOLS, POLY-HYDROXY BENZENES

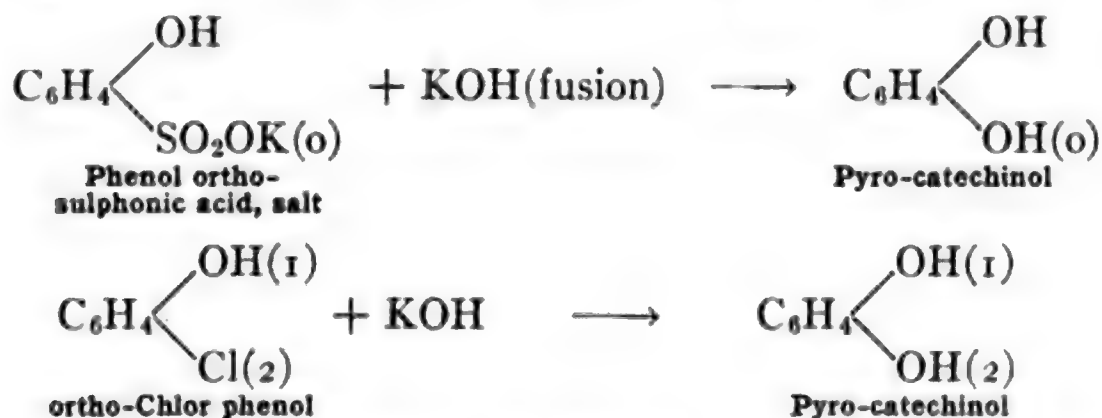
The *poly-phenols* or *poly-hydroxy* benzenes are obtained from the dry distillation products of wood. The methods of synthesis are in general those for the mono-phenols though the diazo reaction does not usually work well with amino phenols. Also some of the methods of preparation used for poly-phenols do not apply to the mono-phenols. In general properties they resemble the mono-compounds, but they are usually more easily soluble in water, react more readily and are characterized by their strong reducing properties.



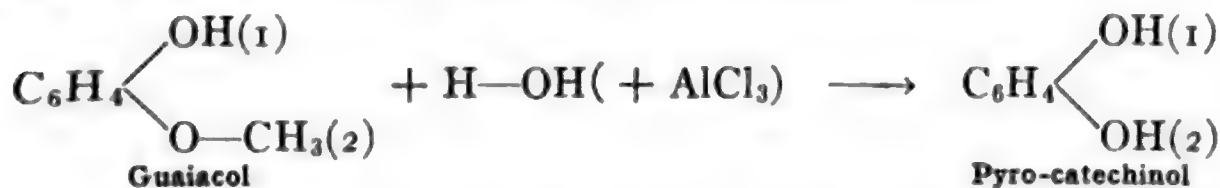
All three of the isomeric *di-hydroxy benzenes* are known and their respective constitutions have been established through their relationships to the three **xylenes** and the three **phthalic acids** (p. 687).

Pyro-catechinol, 1-2-Di-hydroxy Benzene.—The *ortho-di-hydroxy* benzene is known as **pyro-catechinol** or pyro-catechin. The first name is preferable as the termination *ol* indicates its phenol character. Its name also indicates its relation to a resin known as *catechu*, obtained from an *acacia* tree. On distillation it yields the phenol, the prefix *pyro* meaning *heat*. It is also present in the dry distillation products of wood, coal or bituminous shale. Various plant materials such as resins and the leaves of *ampelopsis* yield it by alkali fusion. It is also associated with phenol as a sulphuric acid ester in the urine of horses.

The best methods of synthesis are the potash fusion of **phenol ortho-sulphonic acid** and from **ortho-chlor phenol** with alkali.



Guaiacol.—Another common method of preparing this phenol is from one of its derivatives known as **guaiacol**, a naturally occurring substance (p. 621). It is the methyl ether of the di-phenol which it yields on heating with water and aluminium chloride.



Pyro-catechinol is a crystalline compound; m.p. 104°, b.p. 240°. With ferric chloride it gives a green color, which, on the addition of sodium carbonate or acetate, turns violet. This color test is characteristic of ortho-di-hydroxy compounds. It reduces Fehling's solution.

Resorcinol, 1-3-Di-hydroxy Benzene.—The **meta-di-hydroxy benzene** is known as **resorcinol** or **resorcin**. It is also obtained from plant resins by alkali fusion. Synthetically it is prepared from **phenol meta-sulphonic acid** and from **meta-chlor phenol**. In the case of chlor phenol the *para* compound also yields **meta-di-hydroxy benzene** due to position rearrangement.

Resorcinol is a crystalline compound; m.p. 119° , b.p. 276.5° . It reduces Fehling's solution like the ortho compound, but it differs from the latter in that while it gives a color test with ferric chloride the color is destroyed by adding sodium carbonate.

Fluorescein.—It is an important compound in its reaction with **phthalic anhydride**, yielding beautiful dyes known as **fluorescein** and **eosine**. Hydroxy azo compounds formed from it, however, are not valuable as dyes.

Orcinol, 1-Methyl 3-5-Di-hydroxy Benzene.—The meta di-hydroxy derivative of the benzene homologue toluene, *i.e.*, **1-methyl 3-5-di-hydroxy benzene**, is important because of its relation to the common indicator **litmus**. It is known as **orcinol** taking its name from a species of lichen called *orcina* from which it is obtained by the fermentation of glucosides present in the lichen. Resorcinol being a similar compound takes its name from the same source. When various lichens in their young stage are allowed to ferment, in the persence of ammonia, potash or chalk and atmospheric oxygen, a hydrolytic splitting of the glucosides of the lichen occurs, together with oxidation and reaction with ammonia. The resulting products are dyestuffs termed *orceill dyes* from the principal constituent, **orcein**.

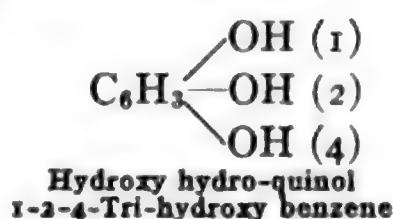
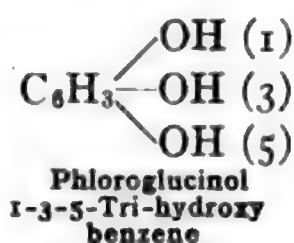
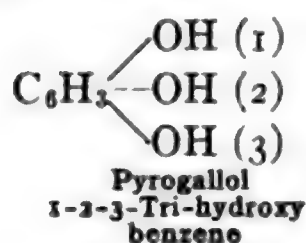
Litmus.—One of the dyes so obtained is the indicator **litmus**. Orcinol does not yield fluorescein dyes with phthalic anhydride.

Hydro-quinol, 1-4-Di-hydroxy Benzene.—The third isomeric di-hydroxy benzene, viz., the para compound, **1-4-di-hydroxy benzene**, is known as **hydro-quino** or **hydro-quinone**. The latter name is derived from its relation to **quinone** (p. 636) from which it is obtained on reduction and which it yields on oxidation. Both hydro-quinol and quinone derive their names from the fact that they are obtained by the oxidation of **quinic acid**, an acid derived from the alkaloid **quinine**. The phenol is found in various plants or may be obtained from them by the hydrolysis of glucosides present, *e.g.*, **arbutin**, which is a glucoside hydrolyzing into **glucose** and **hydro-quinol**.

Hydro-quinol may be synthesized by any of the general methods. Of special interest is its synthesis by the electrolytic oxidation of benzene. It crystallizes in colorless prisms, m.p. 170° . With ferric chloride it gives no color reaction, but is oxidized to **quinone**, the same oxidation occurring in the air in alkaline solutions. It reduces **Fehling's** solution and its important use is as a reducing agent in photography.

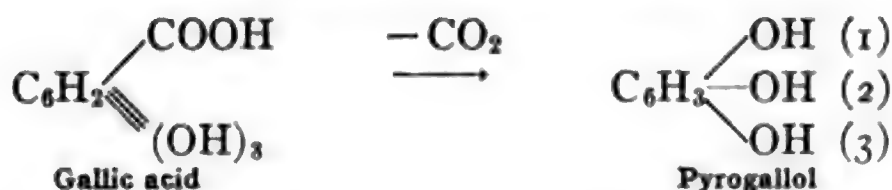


The three isomeric *tri-hydroxy benzenes* are all known.



Only two of these will be considered in detail. Hydroxy hydro-quinol, so named because it is the only possible tri-hydroxyl compound derived from hydro-quinol, is not of special importance.

Pyrogallol.—Pyrogallol, the vicinal or **1-2-3-tri-hydroxy benzene**, is also called **pyro-gallic acid** as it is obtained by heating gallic acid which is a **mono-carboxy tri-hydroxy benzene**.



It is obtained as a product of wood distillation, being present in wood creosote as a *di-methyl ether*. It may be prepared by the general methods of synthesizing phenols. Its most interesting synthesis is by the oxidation of phenol by fusion with sodium hydroxide, but not with potassium hydroxide. It is a white crystalline compound, m.p. 132° , easily soluble in water. It is readily oxidized especially when in alkaline solution. The chief uses of it are due to this strong reducing property.

Gas Analysis.—One use of it is in gas analysis for the determination of oxygen. When air or an oxygen containing gas mixture is passed through an alkaline solution of pyrogallol all of the oxygen is

quantitatively absorbed and the amount present may be calculated from the diminution of the original volume of gas.

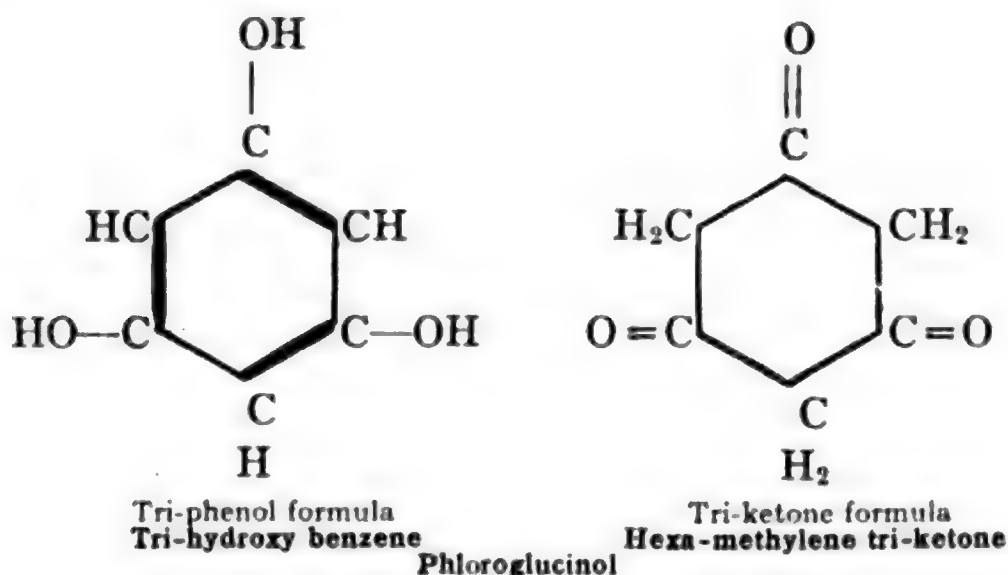
Photographic Developer.—A second important use is as a reducing agent in photographic developers. It also yields a class of dyestuffs.

Phloroglucinol.—The symmetrical or **1-3-5-tri-hydroxy benzene**, is known as **phloroglucinol** or **phloroglucin**. It occurs in many plants and in numerous resins, especially of fruit trees, where it is present in combination as a glucoside, **phloridzin**. This glucoside hydrolyzes with alkalis to **glucose** and **phloretin**. Phloretin is a condensation product of *ortho*-hydroxy hydratropic acid, an acid related to the alkaloid **atropine** (p. 895) and phloroglucinol, the latter being obtained by treatment of the phloretin with alkalis. The phenol is prepared synthetically from **benzene 1-3-5-tri-sulphonic acid** by potash fusion or from **1-3-5-tri-nitro benzene** by reduction to the tri-amino compound, followed by diazotization and decomposition of the diazo compound with water. It may also be made by oxidation of **resorcinol** or **1-3-di-hydroxy benzene** by fusion with sodium hydroxide. Phloroglucinol crystallizes in plates with two molecules of water which are lost at 100°, m.p. 217°. It is soluble in water and has a sweet taste. This fact and its relation to phloridzin gives the name to the compound. It gives a color reaction with ferric chloride and reduces **Fehling's** solution. Like pyrogallol an alkaline solution of it absorbs oxygen from the air.

Pentosan Reagent.—With **furfural** (p. 853) it forms an insoluble greenish black **phloroglucid** compound. As *pentosans* (p. 338) yield furfural on boiling with hydrochloric acid, phloroglucinol is used as a reagent for the determination of the furfural obtained and from this the amount of pentosan is calculated empirically. This is the official method for determination of pentosans in food stuffs.

Constitution. Tautomerism.—The constitution of each of the poly-phenols which we have considered has not been taken up because it has been sufficiently established by the syntheses and reactions as given. In the case of phloroglucinol, however, we have another case of tautomerism. Its constitution as *tri-hydroxy benzene* is established by the syntheses given for it and the fact that it yields *tri-acyl* derivatives. Toward other reagents, however, it acts otherwise than as a hydroxyl compound. Hydroxylamine, $\text{H}_2\text{N}-\text{OH}$, which is the characteristic reagent for aldehydes and ketones (p. 124), yields a

tri-oxime indicating that the compound is a *tri-ketone*, i.e., contains three carbonyl groups ($=\text{CO}$). The two tautomeric formulas are, therefore,



DERIVATIVES OF PHENOLS

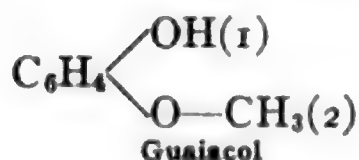
As hydroxyl substitution products possessing both acid and alcohol properties the phenols yield *salts*, *esters* and *ethers*. The salts and esters have been sufficiently considered. The ethers of phenols, especially of those which contain an unsaturated side chain, include several important compounds.

Phenol Ethers, Aryl—O—Alkyl

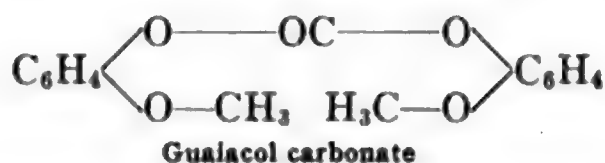
We have already mentioned the methyl and ethyl ethers of phenol, viz., **phenyl methyl ether** or **anisole** and **phenyl ethyl ether** or **phenetole** (p. 612).

Guaiacol.—A phenol ether which needs more detailed mention is the *mono-methyl ether* of *pyrocatechinol* which is known as **guaiacol**. We have stated that with water in the presence of aluminium chloride guaiacol yields **pyrocatechinol** or **1-2-di-hydroxy benzene**,

$\text{C}_6\text{H}_4 \begin{cases} \text{OH}(1) \\ \text{OH}(2) \end{cases}$. Also by reduction with zinc it yields **anisole** or **phenyl methyl ether**, $\text{C}_6\text{H}_5\text{—O—CH}_3$. These two reactions prove its constitution as:



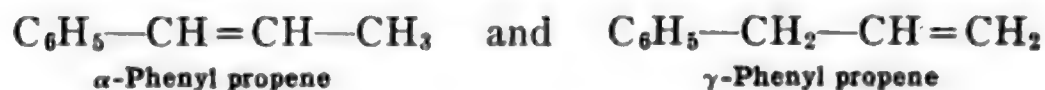
Guaiacol derives its name from the fact that it is obtained by the distillation of a resin known as *guaiac*. It is also similarly obtained from beech wood. It yields a neutral ester with carbonic acid.



This compound possesses medicinal properties and at one time was considered as a remedy for tuberculosis.

Phenols with Unsaturated Side Chain.—At the close of the discussion of the mono-phenols we mentioned the fact that phenols derived from benzene homologues containing an *unsaturated* side chain are known. These will now be considered briefly in connection with their ether derivatives which are the more important compounds. The hydrocarbons of the benzene series which contain an *unsaturated side chain* instead of a saturated one and which have been mentioned are **phenylethylene**, $\text{C}_6\text{H}_5\text{—CH=CH}_2$; **phenylpropenes**, $\text{C}_6\text{H}_5\text{—CH}_2\text{—CH=CH}_2$, $\text{C}_6\text{H}_5\text{—CH=CH—CH}_3$, and **alpha-phenyl propene**, $\text{C}_6\text{H}_5\text{—C}\equiv\text{C—CH}_3$. Phenols, *i.e.*, ring hydroxyl substitution products of these hydrocarbons, are of special importance in that their *ether derivatives* are constituents of some *essential oils*. These oils which are also known as *ethereal oils* are products obtained from the leaves, flowers or fruit of many plants, *e.g.*, *anis seed oil*, *estragon oil*, *fenchel oil*, *oil of cloves*, *bay oil*, *oil of sassafras*, etc.

Isomerism.—The above hydrocarbons in which the unsaturated side chain contains more than two carbon atoms exist in isomeric forms depending upon the position which the benzene ring occupies in the unsaturated chain or, which is the same thing, the *position of the double or triple bond* in the side chain. Thus two **phenyl propenes** are known,



In the phenols and phenol ethers derived from these hydrocarbons this isomerism is of special importance. In many cases one isomer may be converted into the other by simple heating with alcoholic potassium hydroxide. In such a conversion there is a shifting of the position of the double bond.

Anol and Anethole.—The *para* hydroxyl derivative of **alpha-phenyl propene** is known as **anol**. The methyl ether of anol is known as **anethole**.¹



Anol
para-Hydroxy α -phenyl propene



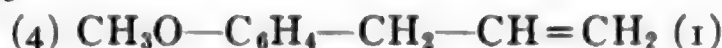
Anethole
para-Methoxy α -phenyl propene

Anethole is a constituent of of *anis seed oil*.

Chavicol and Estragole.—The *para* phenol isomeric with anol is known as **chavicol** and is found in *betel leaf oil*. Its methyl ether is **estragole** which is a constituent of *estragon oil*.



Chavicol
para-Hydroxy γ -phenyl propene

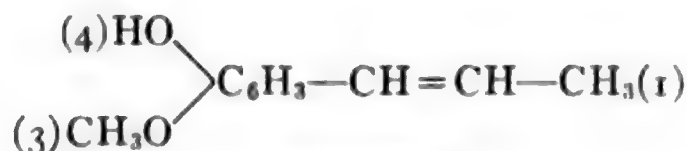


Estragole
para-Methoxy γ -phenyl propene

Eugenole and Safrole.—The chief constituent of a more common essential oil is **eugenole** which occurs in *oil of cloves*. It is the *mono-methyl ether* of **di-hydroxy γ -phenyl propene** in which the methoxy group is *meta* and the hydroxyl group is *para* to the propene chain. It is thus a propene derivative of the mono-methylether of **pyro-catechinol**. The *alpha* isomer is known as **iso-eugenole**.



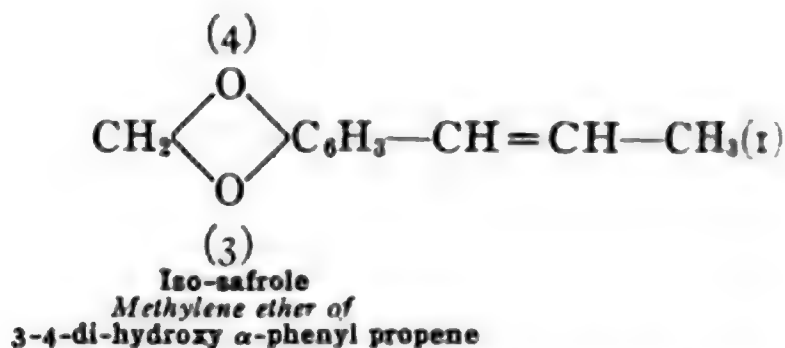
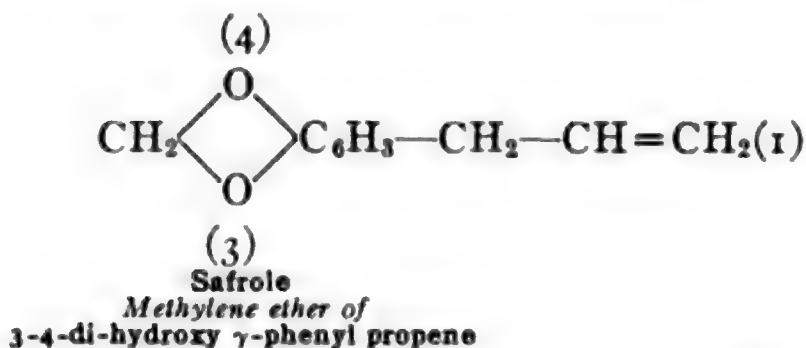
Eugenole
4-Hydroxy 3-methoxy
 γ -phenyl propene



Iso-eugenole
4-Hydroxy 3-methoxy
 α -phenyl propene

¹ The termination *ole* is used to distinguish from the phenol with the termination *ol*. Usually however, the customary spelling of the essential oil constituents is without the final *e*.

The *methylene ether* corresponding to eugenole is known as **safrole** and is the chief constituent of *oil of sassafras*. Its *alpha* isomer is **iso-safrole**.



The conversion of eugenole into iso-eugenole and of safrole into iso-safrole is accomplished by boiling with alcoholic potassium hydroxide. The oxidation products of these ethers are other important essential oil constituents. **Eugenole** yields the corresponding aldehyde which is known as **vanillin**, the chief constituent of *vanilla beans* from which vanilla extract is made. **Safrole** by oxidation yields a compound known as **piperonal** also as heliotropine. It has the odor of heliotrope flowers and is used as *artificial* heliotrope essence. These latter compounds and also constituents of other essential oils will be considered in detail later in their proper chemical relationship (p. 661, etc.).

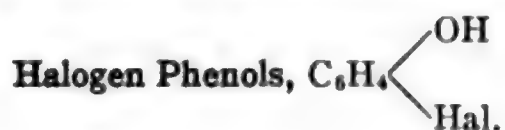
SUBSTITUTED PHENOLS

The substituted phenols result from the substitution of an additional element or group in the original benzene ring. Derivatives of only the mono-phenols will be mentioned. Considered as benzene derivatives these compounds will be poly-substitution products and, therefore, possible of existence in isomeric forms. We thus shall have:

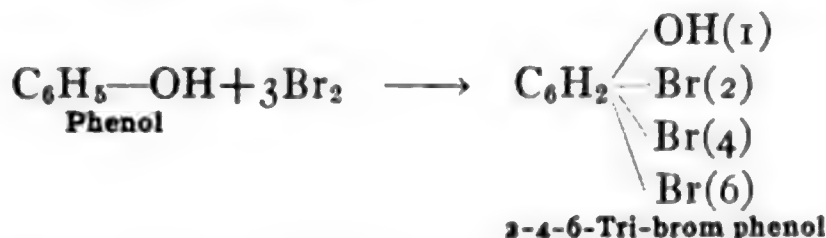
Halogen-hydroxy benzenes	or <i>halogen phenols</i> .
Sulphonic acid-hydroxy benzenes	or <i>phenol sulphonic acids</i> .
Nitroso- and nitro-hydroxy benzenes	or <i>nitroso and nitro phenols</i> .
Amino-hydroxy benzenes	or <i>amino phenols</i> .

We may also have phenols with an aldehyde group or with a carboxyl group in the ring. These will be considered under *hydroxy aldehyde* and *hydroxy acid* compounds. Cyanogen may likewise be the additional substituting group, but as such compounds are nitriles of the hydroxy acids they too will be taken up later in connection with these acids. We have then the four groups of compounds first mentioned to consider at this time.

General Methods of Synthesis.—The general methods of synthesis are two: (1) **From phenols** by direct substitution of some other element or group in the ring of a phenol. As the presence of a side chain in the ring, in the case of the homologues of benzene, makes the compound more easily susceptible to the substitution of other groups, so, likewise, the presence of the hydroxyl group in the ring makes further substitution more easy. Thus nitro phenols and phenol sulphonic acids are more easily prepared by the action of nitric or sulphuric acid on phenols than are the corresponding derivatives of the hydrocarbons themselves, by the similar direct action of the acids on the hydrocarbons. (2) **From substituted sulphonic acids or amines.** By starting with the necessary substituted sulphonic acid, by fusion with potassium hydroxide the sulphonic acid group is replaced by the hydroxyl group and the substituted phenol results. Similarly if a substituted amino benzene is diazotized and then decomposed with water the diazo group which resulted from the original amino group is replaced by the hydroxyl group and we obtain the substituted phenol.



While the introduction of halogens into benzene takes place only with the aid of carriers, phenol reacts with chlorine or bromine at ordinary temperatures yielding *chlor* or *brom phenols*. By the action of bromine water on phenol the product is **tri-brom phenol**.

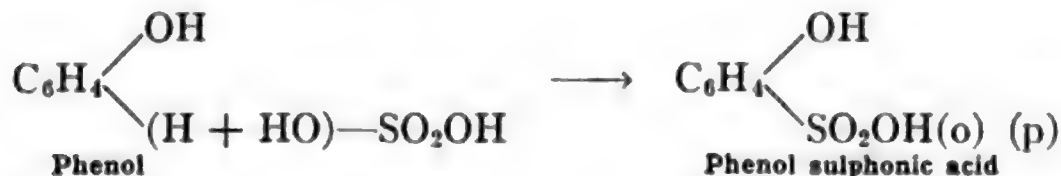


This compound is a characteristic product crystallizing in fine needles and its formation is used as a test for phenol.

The chlor phenols are best formed by the action of **sulphuryl chloride**, SO_2Cl_2 , on phenol. Iodine does not act directly on phenol, but in the presence of **hydriodic acid**, HI , or **mercuric oxide**, HgO , reaction occurs and iodine is substituted in the ring. The halogen phenols are more strongly acid than phenol itself. Fusion of a halogen phenol with alkali replaces the halogen with hydroxyl and a poly-phenol results. In this reaction position rearrangement of the substituting groups often takes place. All of the five remaining hydrogen atoms of the benzene ring in phenol have been replaced by chlorine or bromine or a mixture of the three halogens. Many of the halogen derivatives of phenol and also the salts, esters and ethers derived from them are known, but are not of sufficient importance to be considered further. This is also true of the halogen derivatives of the higher mono-phenols.



The sulphonation of phenol takes place easily on treating it with concentrated sulphuric acid.

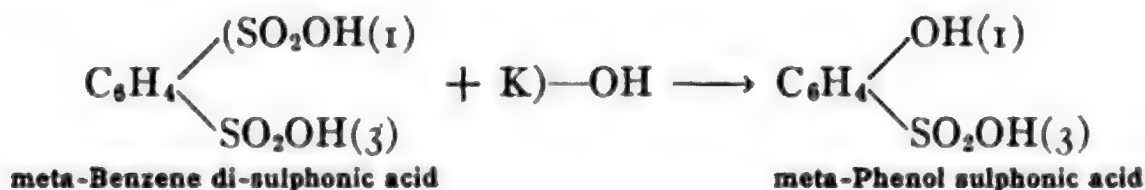


Phenol sulphonic acid is isomeric with the sulphuric acid ester of phenol or phenyl sulphuric acid, the difference being that already discussed as existing between sulphonic acids and sulphuric acid esters (p. 515).

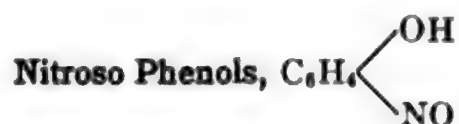


At ordinary temperatures the sulphonation of phenol yields mostly the *ortho* compound with some of the *para*. At raised temperatures the *para* compound only is obtained, the first formed *ortho* compound being converted into the *para*. The *meta* compound is not formed by direct sulphonation of phenol. As previously stated (p. 522), the alkali fusion of di-sulphonic acids yields the di-phenols. By careful fusion

at 170° – 180° it is possible to replace only one of the sulphonic acid groups with hydroxyl and in this way obtain the phenol sulphonic acid. Thus **meta-phenol sulphonic acid** results from such fusion of **meta-benzene di-sulphonic acid**.



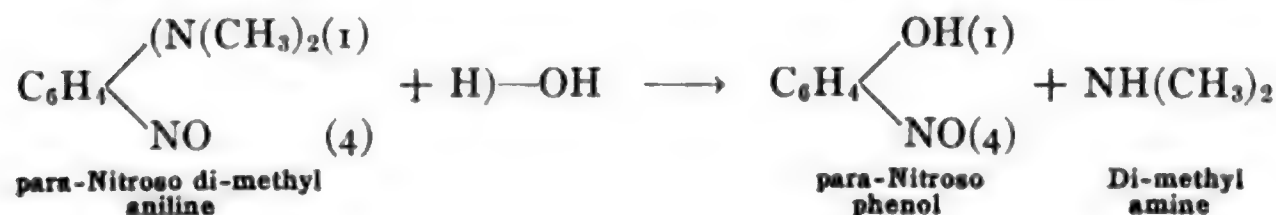
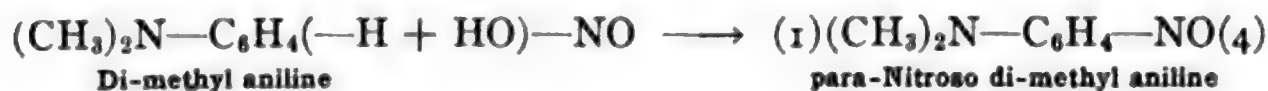
It is interesting that the *para* benzene di-sulphonic acid also yields the *meta* phenol sulphonic acid due to position rearrangement. This same rearrangement, it will be recalled, occurs in the stronger fusion of the *para* di-sulphonic acid, *meta* di-phenol being obtained (p. 522). **Amino benzene sulphonic acid** may also be converted into phenol sulphonic acid by diazotization and decomposition of the diazo compound with water.



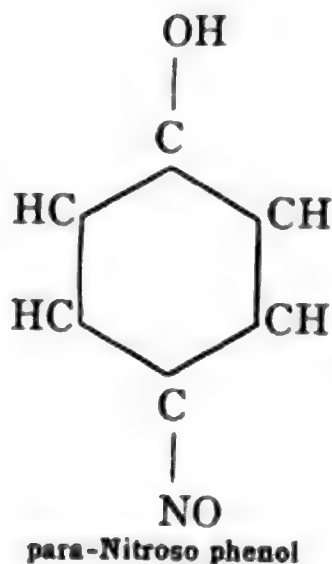
When phenol is treated with nitrous acid, HO—NO , the **nitroso group** enters the ring in the *para* position.



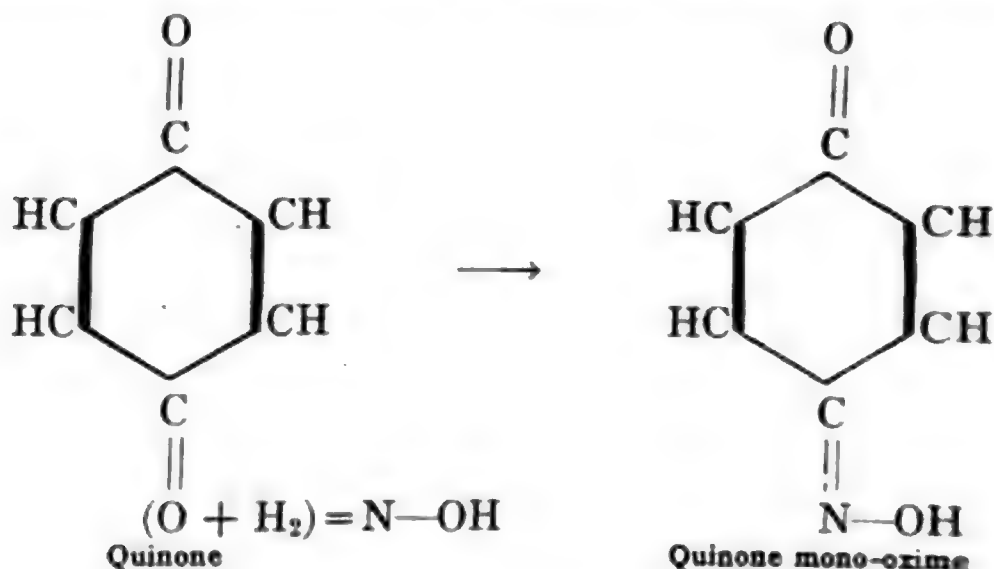
The constitution is proven by the fact that the compound may be prepared from **para-nitroso di-methyl aniline** which is the characteristic product of the reaction of nitrous acid on **di-methyl aniline** (p. 553).



Therefore the constitution is

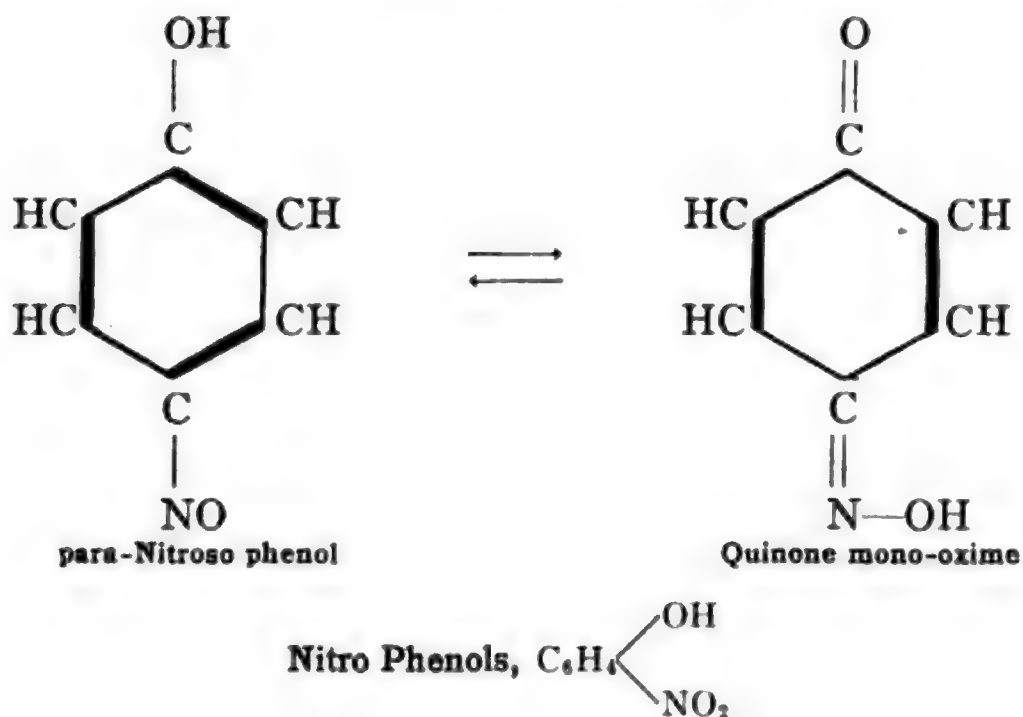


Quinone Oxime.—However, the same compound may be obtained by a wholly different reaction. **Quinone** is a *di-ketone* derivative of benzene related to **hydroquinol** (p. 636). Its constitution by this relationship is as given below. Now when this di-ketone is treated with **hydroxyl amine** which is the characteristic reagent for aldehydes and ketones, yielding *oximes*, we obtain a *mono-oxime* as follows:

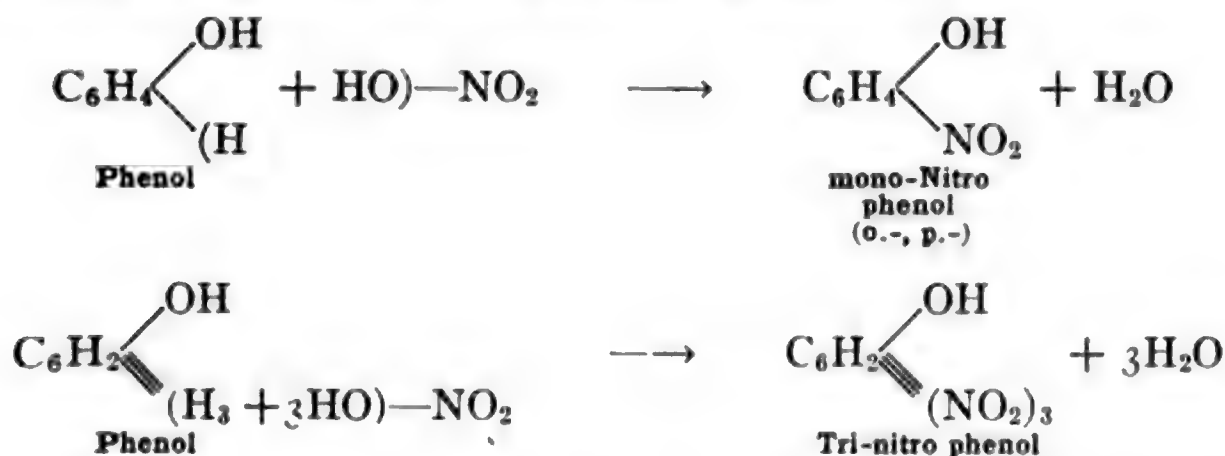


Now this mono-oxime of quinone which must have the above constitution is *identical* with **para-nitroso phenol**.

Pseudo Compounds.—We have then another case of *tautomerism*, the compounds in this case being termed *pseudo compounds*, *i.e.*, compounds apparently different but which exist in the free condition in only one structural form, molecular rearrangement occurring between them.

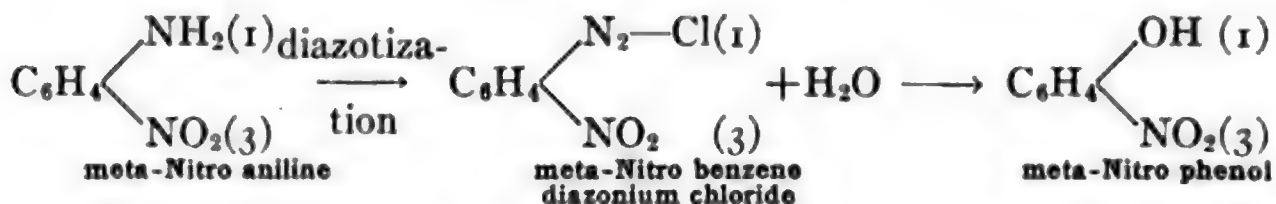


The nitro derivatives of phenols are even more easily formed than the nitro derivatives of the hydrocarbons which, as will be recalled, are readily formed by the action of a mixture of nitric and sulphuric acids upon the hydrocarbon. Even with dilute nitric acid phenol undergoes substitution with the formation of a **mono-nitro phenol** and with concentrated acid a **tri-nitro phenol** results.

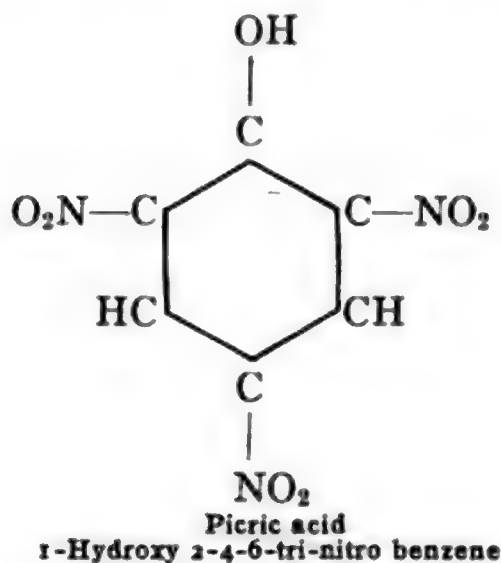


Mono-nitro Phenols.—In the first reaction the product is a mixture of **ortho-nitro phenol** and **para-nitro phenol**. The two may be easily separated as the **ortho** compound is volatile with steam, crystallizing in beautiful yellow crystals, while the **para** compound is not volatile, being left behind when the mixture is distilled with steam. It is then extracted from the residue by boiling with hydrochloric acid, recrystallized from the same solvent and obtained as fine white needles. The preparation and separation of these two compounds is a very satisfactory laboratory exercise. The **meta-nitro phenol** can not be pre-

pared by the direct nitration of phenol but is prepared by the diazo method. **Meta-nitro amino benzene** or **nitro aniline**, $(3)\text{O}_2\text{N}-\text{C}_6\text{H}_4-\text{NH}_2(1)$, is diazotized and the diazo compound decomposed with water, the amino group being thus replaced by hydroxyl.



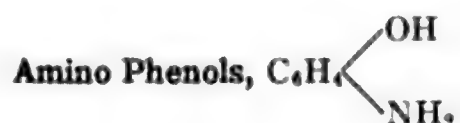
Tri-nitro Phenol. Picric Acid.—When the nitration of phenol is effected with concentrated acid three nitro groups enter the benzene ring and a **tri-nitro phenol** results. The particular tri-nitro compound formed is the symmetrical one and is known as **picric acid**.



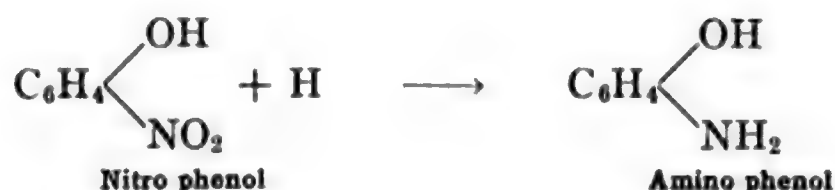
In preparing picric acid the phenol is first converted into a mixture of the **ortho-** and **para-phenol sulphonic acid** (p. 626). This by the action of concentrated nitric acid and heat yields the **tri-nitro phenol**. The nitro phenols are all more strongly acid than phenol itself. **Picric acid** is a yellow crystalline solid, m.p. 122.5° , and has a distinctly bitter taste. It forms an intensely yellow solution in water and the salts are even more strongly colored.

Dyestuff.—Picric acid is a dyestuff, dyeing wool and silk a bright yellow. It was the first chemical dye to be used, but is seldom used now except in connection with other dyes to produce certain shades of color.

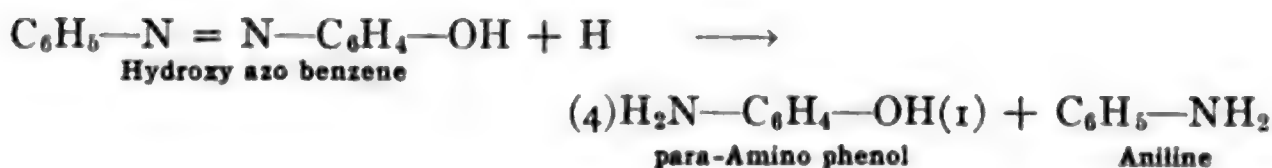
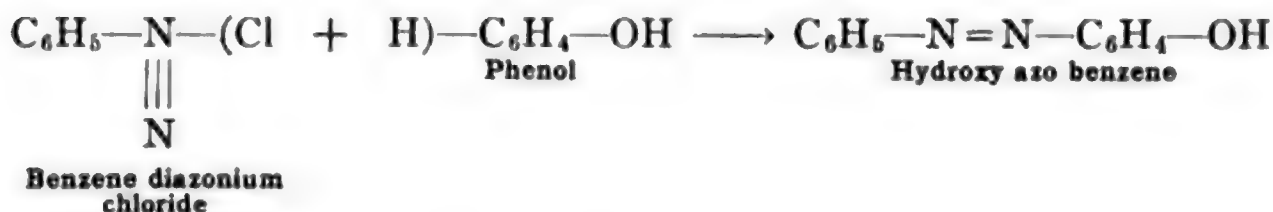
Picrate Explosives.—A most important property of the salts of picric acid, especially **ammonium picrate**, is their explosive character. They are used in the manufacture of certain smokeless powders, *e.g.*, **melinite** and **liddite**. Picric acid itself is not explosive but the salts are exploded either by percussion or ignition. Picric acid is used as an antiseptic and alleviator in the case of burns. It precipitates organic bases and proteins and is used in this way as a test for proteins.



The most important phenol derivatives are the *nitro phenols*, which we have just discussed, and the related *amino phenols*. The amino phenols like the amino hydrocarbons may be formed by the reduction of the corresponding *nitro* or *nitroso* compounds.

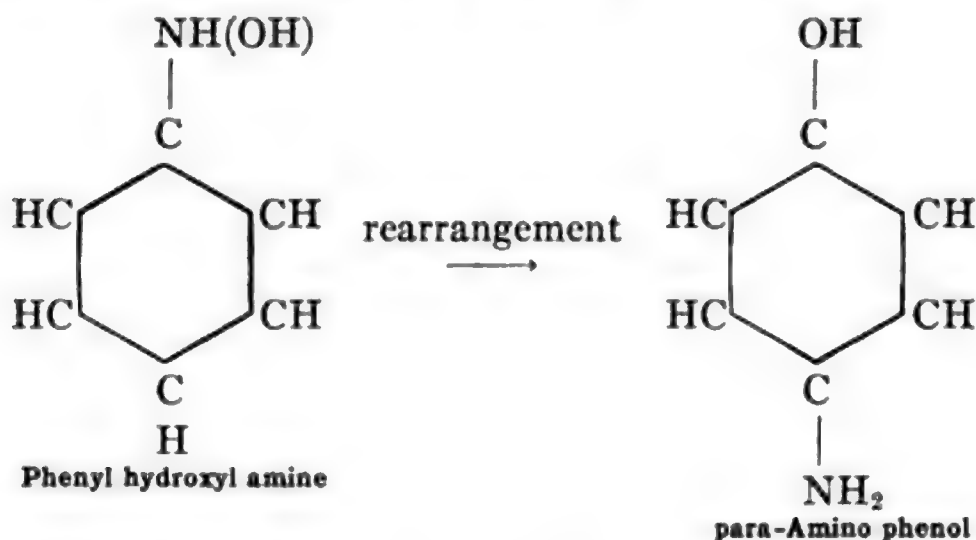


The reduction may be brought about either by means of tin and hydrochloric acid or electrolytically. *Hydroxy azo* compounds also yield amino phenols on reduction, the former being the product of the reaction between a diazonium salt and a phenol. This gives an indirect method of preparing amino phenols from the phenols.

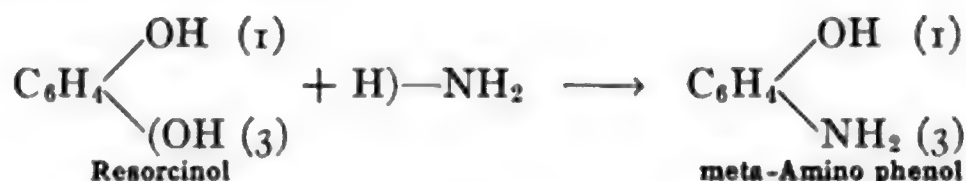


Molecular Rearrangement of Hydroxyl Amines.—An important synthesis of amino phenols is by a *molecular rearrangement* of hydroxyl

amine derivatives. **Phenyl hydroxyl amine** undergoes such a rearrangement and yields **para-amino phenol**.



We have previously stated (p. 612) that mono-phenols have the hydroxyl group replaced by the amino group when they are treated with ammonia zinc chloride. Similarly, with greater ease, the di-phenols may have one hydroxyl group replaced by an amino group when heated with ammonia, thus yielding amino phenols. This method is used in preparing **meta amino phenol** from **resorcinol**, **meta-di-hydroxy benzene**.



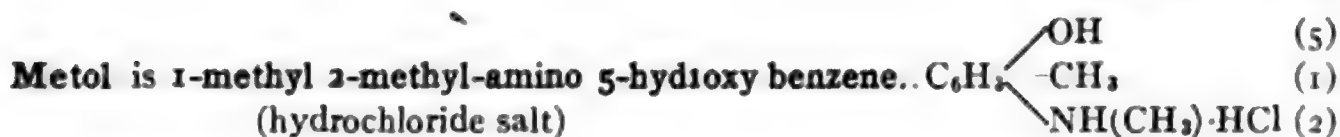
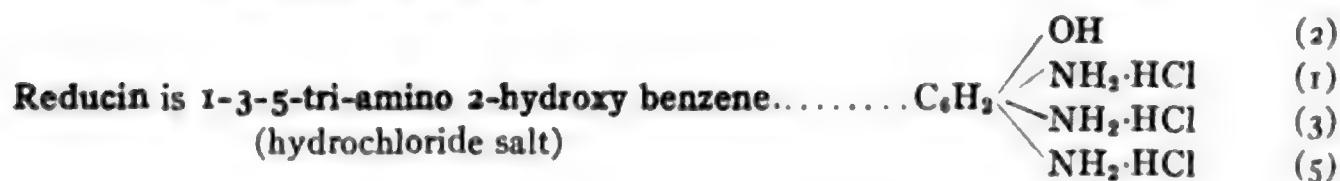
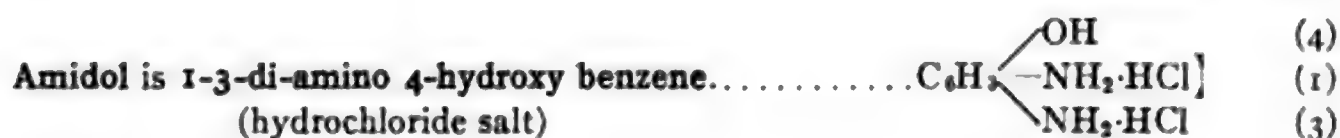
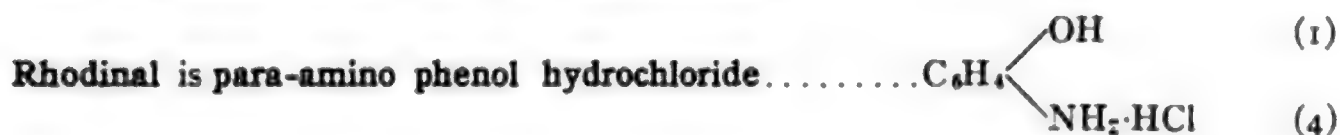
The amino phenols are strongly basic due to the fact that the stronger basic character of the amino group more than counterbalances the acid character of the phenyl radical of the phenol. They, therefore, form

ammonium salts with acids, *e.g.*, $\text{C}_6\text{H}_4 \begin{array}{l} \text{OH} \\ \diagdown \\ \text{NH}_2 \cdot \text{HCl} \end{array}$, **hydroxy phenyl ammonium chloride**, hydrochloride salt of amino phenol.

The amino phenols are easily oxidized, especially in alkaline solution, so that it is impossible to obtain the free amino phenol (base) by treatment of the salt with potassium hydroxide. To obtain the free base from the salt we, therefore, use sodium acid carbonate or sodium sulphite.

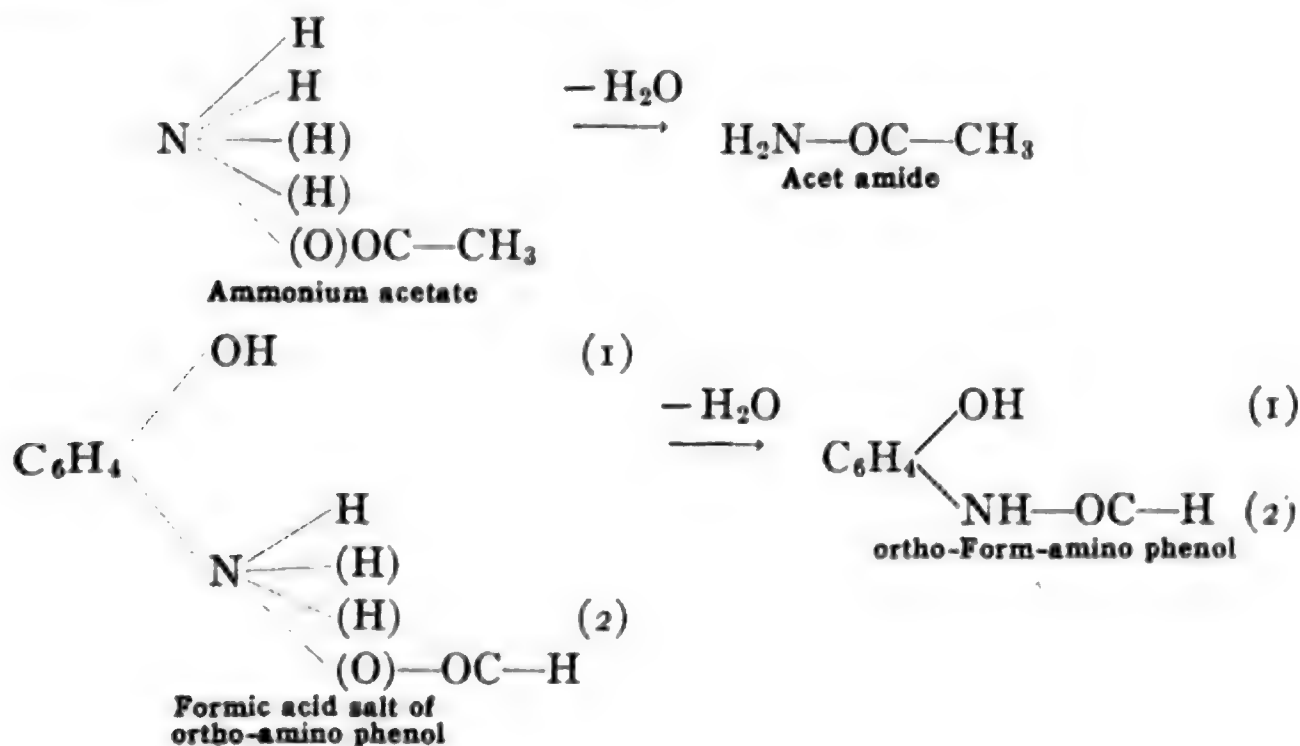
Photographic Reducing Agents.—The property of easy oxidation gives to the amino phenols an important use as reducing agents in

photographic developers. A few of the amino phenol compounds thus used in photography may be mentioned.

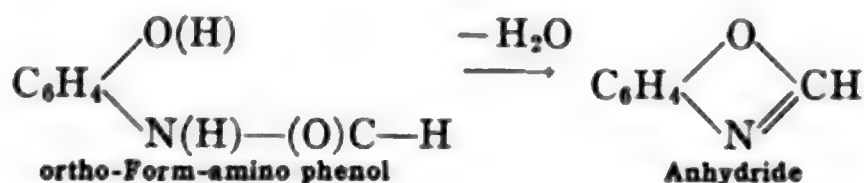


Ethers.—As phenol compounds, the amino phenols yield phenol ethers analogous to **phenetole** (p. 621). These ethers are themselves unimportant.

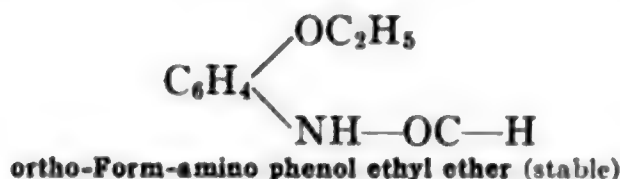
Acid Amide Derivatives.—As amines, the amino phenols yield, with organic acids, compounds of the *acid amide* type like **acet amide**, $\text{CH}_3\text{—CO—NH}_2$. The compounds first formed with the organic acids are probably salts analogous to the hydrochloride salt. These, however, readily lose water, just as ammonium acetate does with more difficulty, and yield the acid amide.



This acid amide compound however, when the groups are in the *ortho* positions, loses another molecule of water on heating and yields an anhydride.



If, however, the phenol hydroxyl group is converted into the ether the acid amide compound is stable and does not yield an anhydride.



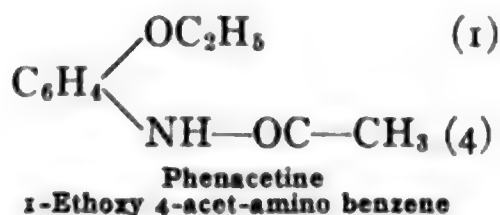
The corresponding *acetyl* derivative is an important medicinal substance.

Phenetidine.—The ethyl ether of phenol is known as **phenetole** and the ethyl ether of **para-amino phenol**, or para-amino phenetole is

similarly named **phenetidine**, $\text{C}_6\text{H}_4 \begin{array}{l} \diagup \text{OC}_2\text{H}_5 \text{ (1)} \\ \diagdown \text{NH}_2 \text{ (4)} \end{array}$. The acetic acid

amide of this compound does not yield an anhydride and is a stable compound.

Phenacetine.—It is known as **phenacetine**, the derivation and significance of the name being apparent from the above relationships.



Phenacetine is an important *antiseptic* and *antipyretic* and is a valuable medicinal substance. It is a solid crystalline compound, m.p. 135° . It is slightly soluble in cold water and in 70 parts of hot water. Other similar derivatives of phenetidine are important. The one formed from **glycine** or **glycocoll**, **amino acetic acid**, $\text{CH}_2(\text{NH}_2)\text{—COOH}$, is

known as **phenocoll**, $\text{C}_6\text{H}_4 \begin{array}{l} \diagup \text{OC}_2\text{H}_5 \\ \diagdown \text{NH-OC-CH}_2(\text{NH}_2) \end{array}$, while the corre-

sponding lactic acid derivative, $\text{C}_6\text{H}_4 \begin{array}{l} \diagup \text{OC}_2\text{H}_5 \\ \diagdown \text{NH-OC-CH(OH)-CH}_3 \end{array}$, is

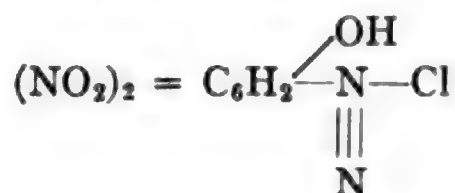
called **lactophenine**. Still one more may be mentioned, viz., the

carbamic acid, HOOC-NH_2 , derivative, $\text{C}_6\text{H}_4 \begin{array}{l} \diagup \text{OC}_2\text{H}_5 \\ \diagdown \text{NH-OC-NH}_2 \end{array}$,

which is called **dulcin** and is a sweet substance two hundred times as sweet as cane sugar, but not as sweet as saccharin (p. 712).

Dyes.—The amino phenols are also important in connection with dyestuffs. Para-amino phenol is itself used in dyeing leather, but in most cases the amino phenols or their derivatives are intermediate products in the formation of compounds used as dyes; in particular certain groups of *azo dyes* and those known as *rhodamine dyes*.

Azo phenols which are of course the same as *hydroxy azo compounds* (p. 576), *azoxy phenols*, *hydrazo phenols*, *phenol hydrazines* and *di-azo phenols* are all known either as phenols or as phenol ethers. The last group is interesting historically as the first diazo compound made by Griess was di-nitro phenol diazonium chloride,



QUINONES

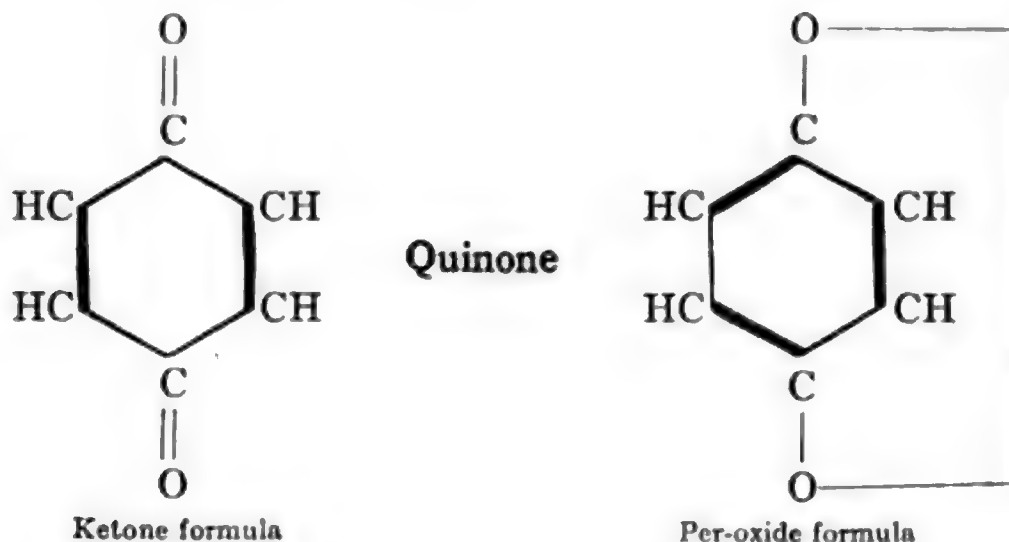
Having now considered those hydroxyl substitution products of benzene and its homologues in which the substitution is in the *ring*, we should next take up the second general class of hydroxyl substitution products, viz., those in which the substitution is in the *side chain*, i.e., the true *alcohols*. Before we take up these compounds, however, it is best to consider here a group related to the phenols and concerning the constitution of which there is still some controversy.

Quinone.—The chief representative of this group is a substance by the name of **quinone**, or more definitely **benzoquinone**, which has the composition $C_6H_4O_2$. It will be recalled that hydroquinone, which is the

para-di-hydroxy benzene, C_6H_4 $\begin{matrix} \text{OH(1)} \\ \text{OH(4)} \end{matrix}$, is made, as its name indi-

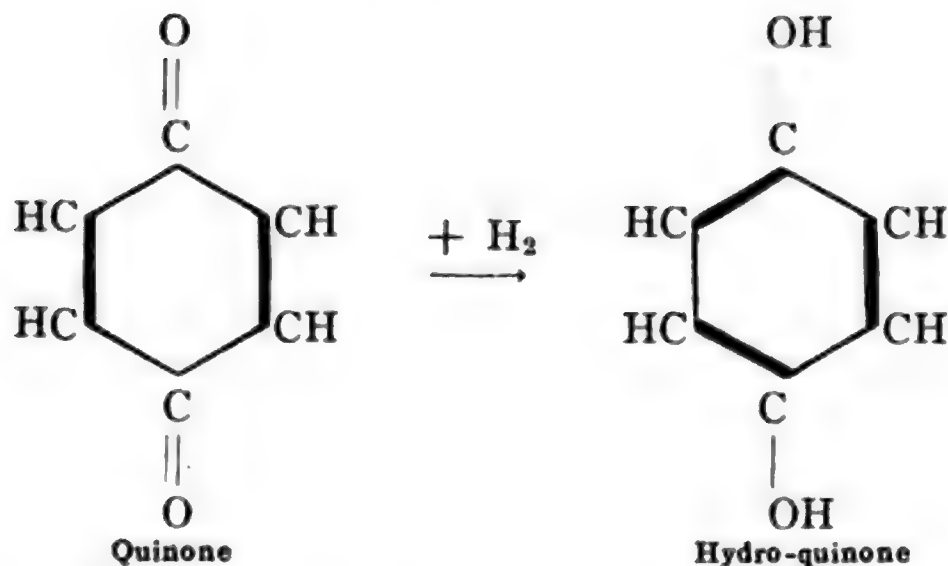
cates, by the reduction of **quinone**. This fact together with the composition of quinone leads to the view that quinone is related to benzene in that two of the benzene hydrogens, **para** to each other, are replaced by two oxygen atoms. These two oxygens on reduction are converted into two hydroxyl groups in hydro-quinone.

Ketone or Per-oxide.—Two different constitutional formulas are possible in accordance with such a relationship, *viz.*, a *ketone* formula and a *per-oxide* formula as follows:



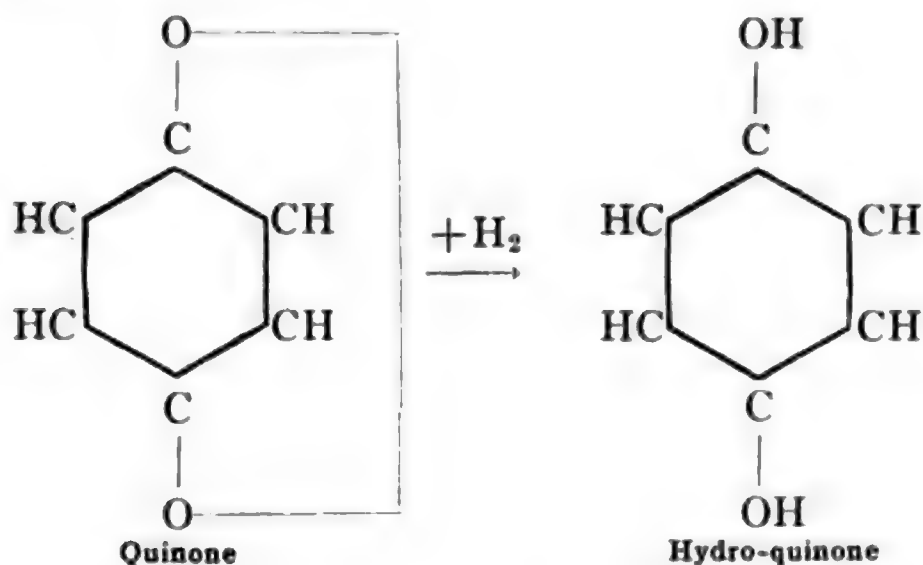
In the ketone structure the two oxygens are united directly to carbon as the carbonyl or ketone group, $=C=O$, whereas in the per oxide structure they are united to the carbons by a single bond, the other valence of the oxygens mutually satisfying each other as in per-oxides.

In order to make the ketone formula possible in accordance with the structure of the benzene ring it is necessary to consider the double bonds as changing or oscillating to the positions indicated in the above formula. When reduction to hydro-quinone occurs the double bonds oscillate back to their original position.



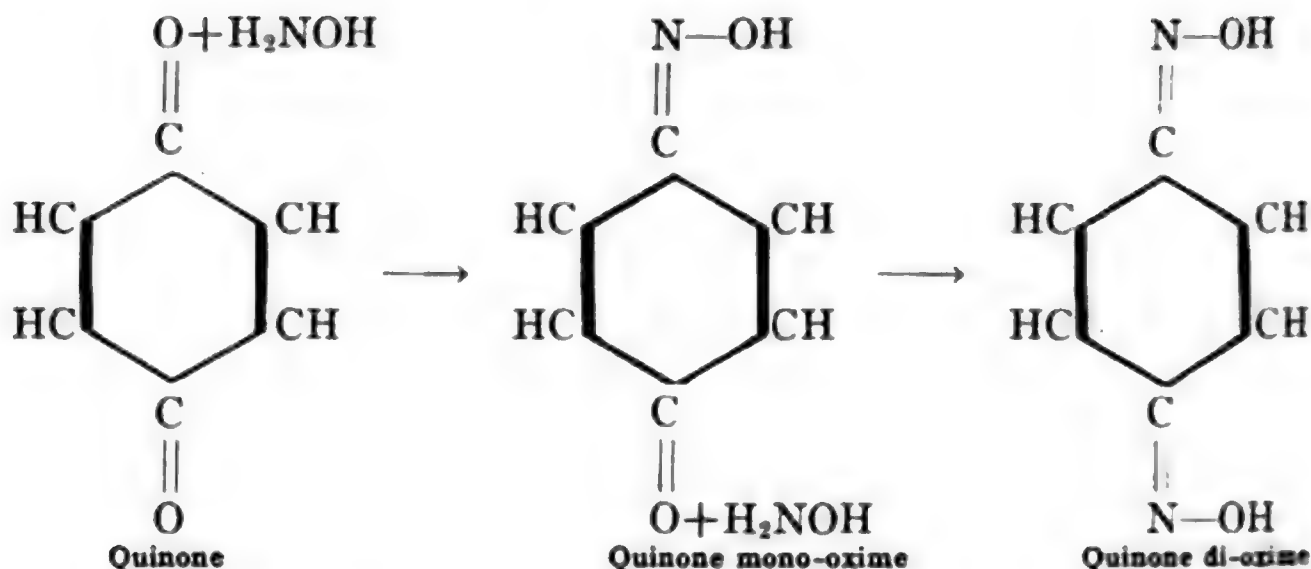
Such oscillation of the double bonds of the benzene ring is one of the assumptions in connection with the **Kekulé** benzene formula as referred to when we were discussing the constitution of benzene (p. 474).

The conversion of a compound with the per-oxide formula into hydro-quinone does not necessitate any oscillation of the double bonds but simply the breaking of the union between the two oxygen atoms with their reduction to hydroxyl.



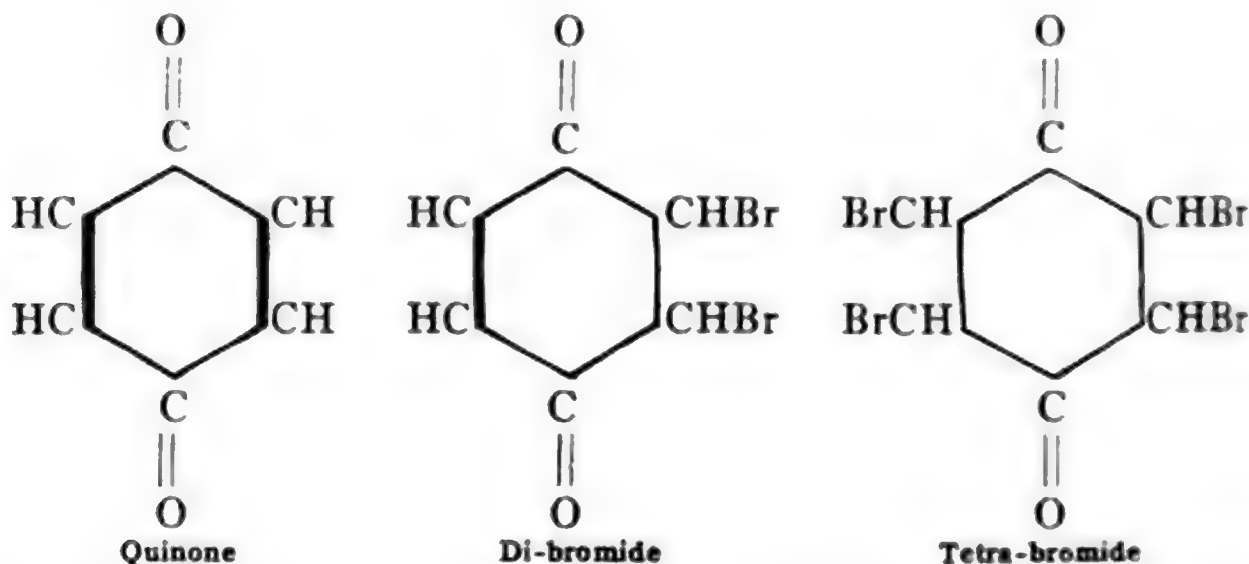
Oximes.—Evidence in favor of the ketone structure is that quinone undergoes the characteristic aldehyde or ketone reaction with hydroxyl amine forming *oximes*. Furthermore, it forms both a *mono*- and a *di*-oxime.





From this it would appear that the two oxygen atoms in quinone are each in the carbonyl grouping and are independent of each other.

Another fact in favor of the ketone structure is that quinone forms *di-* and *tetra-halogen addition products* but not *penta-* and *hexa-* compounds.

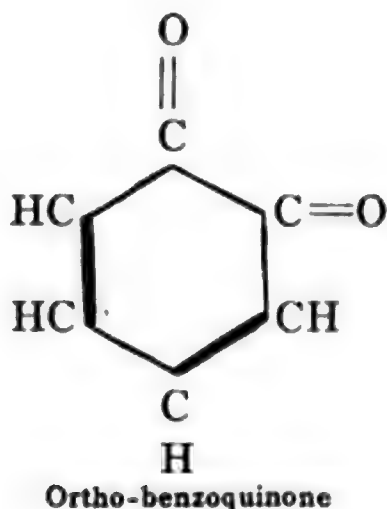


If the per-oxide structure is the true one it would seem possible to form penta- and hexa-brom addition products also.

Benzo-quinone.—**Benzoquinone**, or more commonly, simply **quinone**, is the most common and important of the quinones derived from benzene. Other important quinones will be met with when we study derivatives of the more complex hydrocarbons **naphthalene** and **anthracene**. Benzoquinone is the one we have used as our example in the above discussion and it is the **para-di-keto benzene**. It was first obtained by the oxidation of **quinic acid**, which in turn was obtained from **quinine**, hence its name. It may also be prepared by oxidizing

hydroquinone or **aniline**. It is a crystalline compound, volatile with steam, forming long yellow prisms which sublime as golden-yellow needles. It has a peculiar penetrating odor.

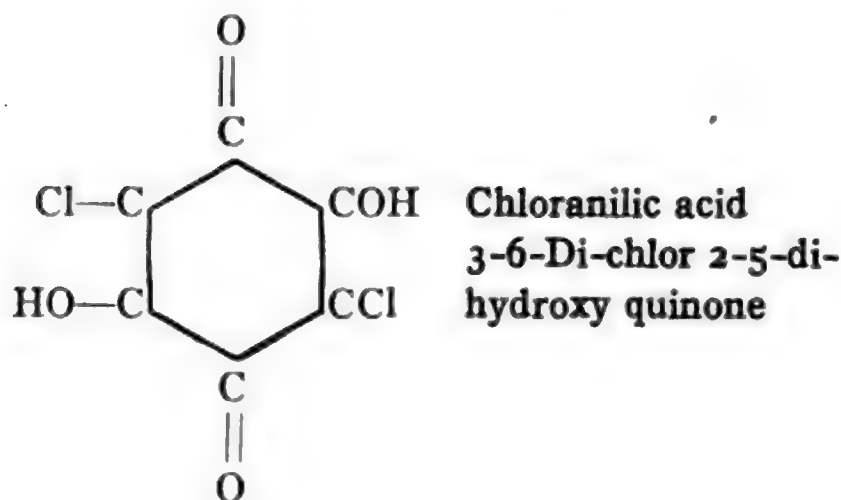
Ortho-quinone.—Corresponding to the common benzoquinone which is the *para* compound, there are known derivatives of the **ortho-benzoquinone**. In this compound, as represented by the ketone formula, no oscillation of the double bonds of the benzene ring is necessary.



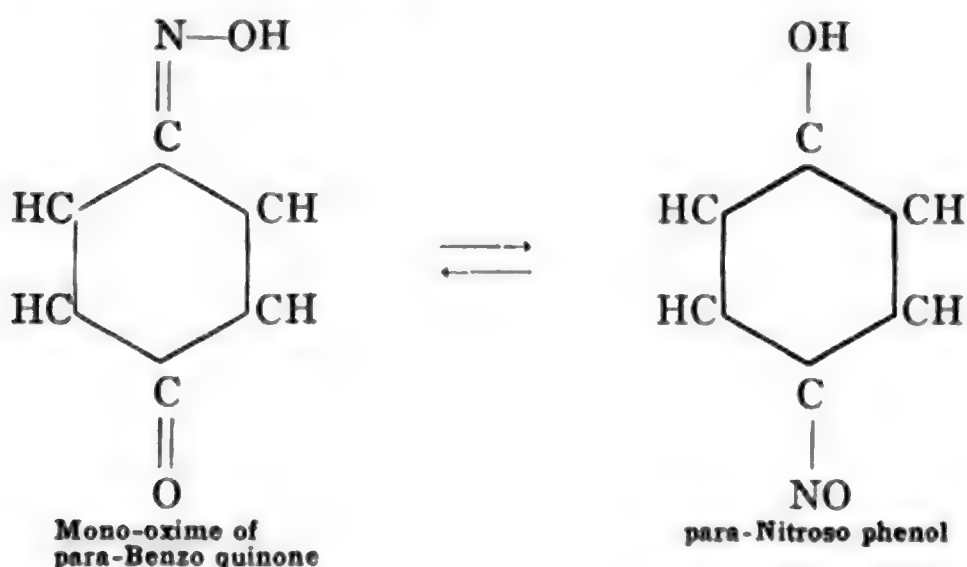
DERIVATIVES OF QUINONES

Chloranil.—We have spoken of the fact that halogen derivatives of quinones are formed as addition products, the di- and tetra-products being known. The halogens form other derivatives also in which the halogen is substituted for hydrogen of the benzene ring. These are true substituted quinones. The tetra-chlor quinone, $C_6Cl_4O_2$, is known as **chlor-anil** and is formed when **aniline** or **phenol** is treated with potassium chlorate and hydrochloric acid.

Chloranilic Acid.—Hydroxyl substitution products of quinone are important as they yield salts with bases which are intensely colored and therefore valuable as dyes. The most important one of these compounds is a *di-hydroxyl* product of a quinone related to **anthracene** and known as **alizarin**. A mixed chlorine and hydroxyl substitution product is the **di-chlor di-hydroxy quinone**. It is chloranil in which two of the chlorine atoms have been replaced by hydroxyl groups, and is known as **chloranilic acid**.



Quinone Oximes.—The most interesting of the derivatives of quinones are the *oximes*. As stated in the discussion of the ketone structure for quinones one of the proofs for this constitution is the fact that benzoquinone forms both a mono- and a di-oxime when treated with hydroxyl-amine. The mono-oxime of benzoquinone would have the structure as written below and as given on page 638. Now as previously mentioned, (p. 628), **para-nitroso phenol**, which is made by the action of nitrous acid upon phenol and the constitution of which is established by other methods of synthesis, (p. 627), proves to be one and the same compound with this **mono-oxime of para-benzoquinone**, the constitution of which is likewise established by the above reaction of hydroxyl amine upon quinone. This is explained by a rearrangement as shown in the following:



Now the following facts: (1) the oxime itself is not known as distinct from para-nitroso phenol, (2) there are known both ethers and esters

derived from it, (3) we do know the corresponding di-oxime; indicate that the mono-oxime of benzo-quinone is really formed, but that either it or the para-nitroso phenol undergoes a rearrangement into the other form. This is a peculiar case of tautomerism as only one compound is known which may be prepared by two entirely different sets of reactions. Such compounds are known as *pseudo compounds*.

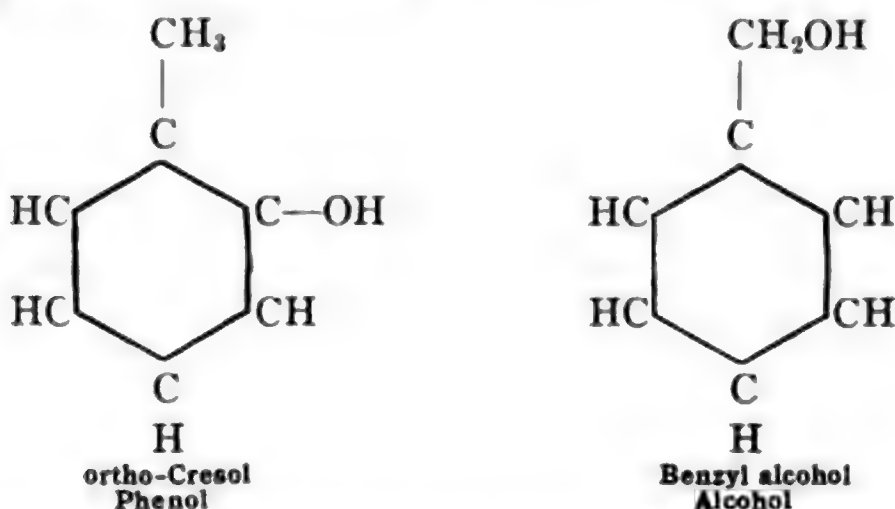
Further discussion of these compounds is unnecessary in this study, but the salient points have been brought out as well as the relation of the quinones to several other classes of compounds.

B. AROMATIC ALCOHOLS

(Hydroxyl in the Side Chain)

MONO-HYDROXY COMPOUNDS

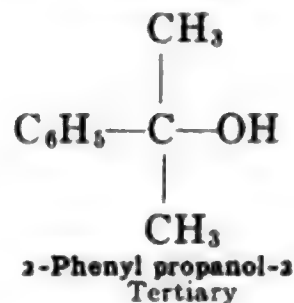
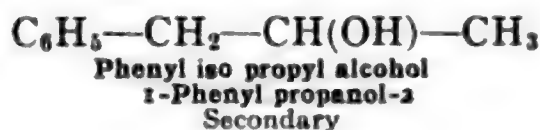
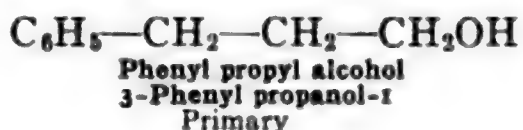
Turning now to the second class of hydroxyl substitution products, the true *alcohols*, we must recognize the essential difference, viz., that in them the hydroxyl group is substituted in the *side chain* whereas in *phenols* it is in the ring. Thus **toluene**, the first benzene hydrocarbon containing a side chain, will yield both a phenol and an alcohol the two being isomeric compounds.



The side chain hydroxyl compounds are true *alcohols* in every respect, in properties, reactions, methods of synthesis and derivatives. They yield, therefore, both *ethers* and *esters*. As alcohols they are of several kinds depending upon the character of the alcoholic side chain and are exactly analogous to the different classes of aliphatic alcohols.

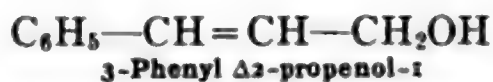
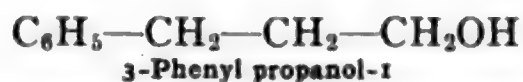
Primary, Secondary, Tertiary.—In the first place they may be either *primary*, *secondary*, or *tertiary* according to the position of the hydroxyl

group in the side chain when this side chain contains more than one carbon group, *e.g.*;

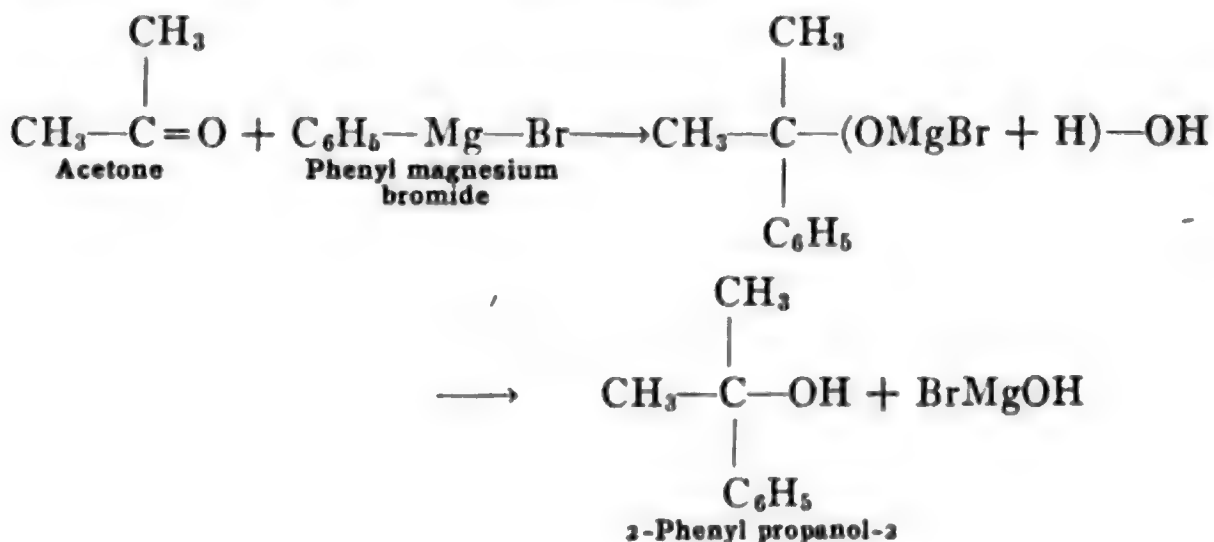


Benzyl alcohol or phenyl methyl alcohol given above can, of course, exist only as a primary alcohol there being only one carbon group in the side chain. Like the aliphatic alcohols, the primary yield aldehydes and then acids on oxidation, the secondary yield ketones and the tertiary break down.

Saturated and Unsaturated.—Again as alcohols they may be either saturated or unsaturated, corresponding to the two classes of benzene homologues, *e.g.*;



Grignard Synthesis.—The most important method for synthesizing aromatic alcohols is by the **Grignard reaction**, with *magnesium alkyl or aryl halides* (p. 77). The one given as an example of a tertiary aromatic alcohol may be prepared by the action of **magnesium phenyl bromide**, $\text{C}_6\text{H}_5\text{—Mg—Br}$, upon **acetone**.

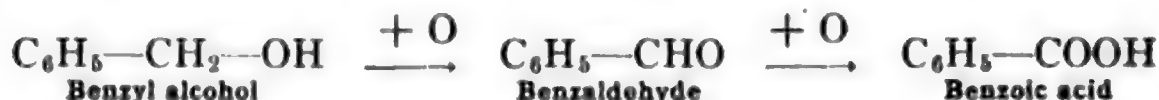


As in the **Grignard reaction** we may use any *aliphatic* aldehyde, ketone, ester or acid chloride, or an *aryl* compound of the same type; and also, we may use either *alkyl magnesium halides* or *aryl magnesium halides*; the synthesis makes possible the preparation of practically any desired secondary or tertiary alcohol either *aliphatic* or *aromatic*. Also if **formaldehyde**, in the form of its polymer, **tri-oxy methylene**, is used in the second reaction we will obtain *primary* alcohols. In the third reaction **formic acid** esters yield *secondary* instead of tertiary alcohols. These syntheses of alcohols by the **Grignard reaction** give us an idea of its importance in synthetic work.

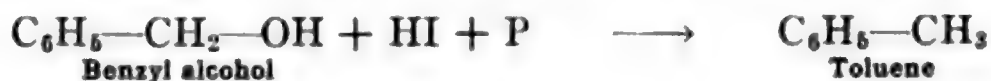
While the preceding syntheses are the most important the simplest synthesis of aromatic alcohols is from the side chain *hologen* substitution products by treatment with silver hydroxide, potassium hydroxide or even by boiling with water.



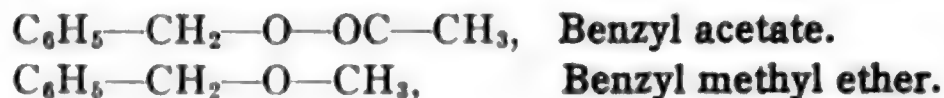
Benzyl Alcohol.—The simplest aromatic alcohol is the hydroxyl derivative of toluene and is known as **benzyl alcohol**, $\text{C}_6\text{H}_5\text{—CH}_2\text{—OH}$. The radical, $(\text{C}_6\text{H}_5\text{—CH}_2\text{—})$, is termed *benzyl* as in the alcohol and chloride above. The alcohol occurs as an ester in Peru balsam, in storax, a resin obtained from a plant styrax, and in Tolu balsam from which the mother hydrocarbon **toluene** derives its name. On hydrolysis of the balsam benzyl alcohol is obtained. It is a liquid, b.p. 206.5° , slightly soluble in water and soluble in alcohol or ether. It may be prepared by those syntheses just given which yield primary alcohols. It may also be prepared by the reduction of the corresponding aldehyde, known as **benzoic aldehyde** or **benzaldehyde** (p. 655). On oxidation it yields the aldehyde and then an acid, **benzoic acid**.



Strong reducing agents reduce it to the hydrocarbon **toluene**.



It yields both esters and ethers, *e.g.*;

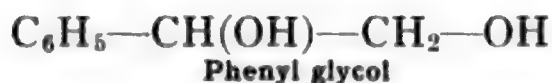
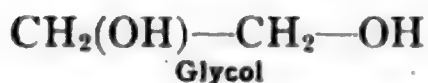
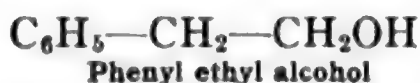


Homologues.—The homologues of benzyl alcohol result from substitution of the hydroxyl group in one of the methyl groups of **xylene**, **mesitylene**, etc., or, as in the examples previously given of secondary and tertiary aromatic alcohols, by the substitution of hydroxyl in a poly-carbon side chain either saturated or unsaturated. These need not be discussed further except to mention that both **phenyl propanol**, $\text{C}_6\text{H}_5\text{—CH}_2\text{—CH}_2\text{—CH}_2\text{OH}$, and **phenyl propenol**, $\text{C}_6\text{H}_5\text{—CH=CH—CH}_2\text{OH}$, are also found as cinnamic acid esters in *storax*.

Cinnamic Alcohol.—The latter alcohol yields an unsaturated aromatic acid known as **cinnamic acid** (p. 697), and the alcohol is thus known as **cinnamic alcohol**. **Phenyl ethyl alcohol**, $\text{C}_6\text{H}_5\text{—CH}_2\text{—CH}_2\text{—OH}$, is a constituent of oil of rose and has the characteristic odor of roses.

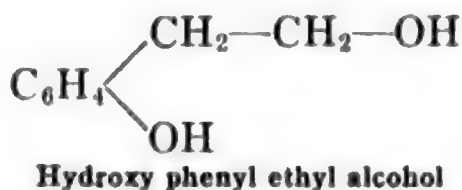
POLY-HYDROXY COMPOUNDS

Aromatic Glycols.—As we have *poly-phenols* which contain more than one hydroxyl group in the ring so we may have *poly-alcohols* containing side chains in which more than one hydroxyl group is present. Those with two hydroxyl groups will be phenyl derivatives of the *glycols* the di-hydroxy aliphatic alcohols.

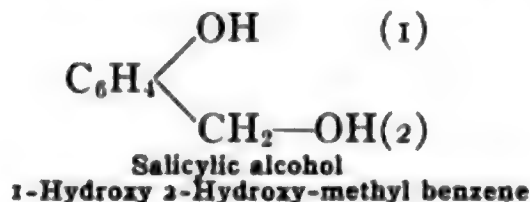


While these compounds are not of especial importance another class of di-hydroxyl compounds does contain some important members.

Phenol Alcohols.—Just as the aromatic alcohols are isomeric with certain phenols, *e.g.*, **benzyl alcohol** and the **cresols**, so a di-hydroxyl compound derived from **phenyl ethane**, in which one hydroxyl group is in the *side chain* and the second one is in the ring, is isomeric with **phenyl glycol**.

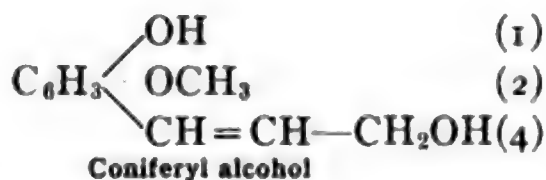


Salicylic Alcohol.—Such a compound is a mixed phenol and aromatic alcohol. The corresponding derivative of methyl alcohol, viz., the *ortho* compound, occurs combined with **glucose** as a *glucoside* known



as **salicin** which is present in willow bark. As we shall find later this alcohol is directly related to **salicylic acid** which it yields on oxidation. It is thus known also as **salicylic alcohol**.

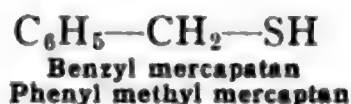
Coniferyl Alcohol.—If two hydroxyl groups are present in the ring and one in the side chain we will have a mixed diphenol and aromatic alcohol. Such an alcohol, in which one phenol hydroxyl is in the form of a methyl ether, and the side chain is the **propenol** unsaturated chain, is known as **coniferyl alcohol**.



Coniferyl alcohol like salicylic alcohol occurs as a glucoside in plants, in the cambium sap of conifer trees. The glucoside is known as **coniferin**. On hydrolysis these glucosides yield the alcohols.

Thio-Phenols and Aromatic Mercaptans

Sulphur analogues of phenols and aromatic alcohols are known, *e.g.*,



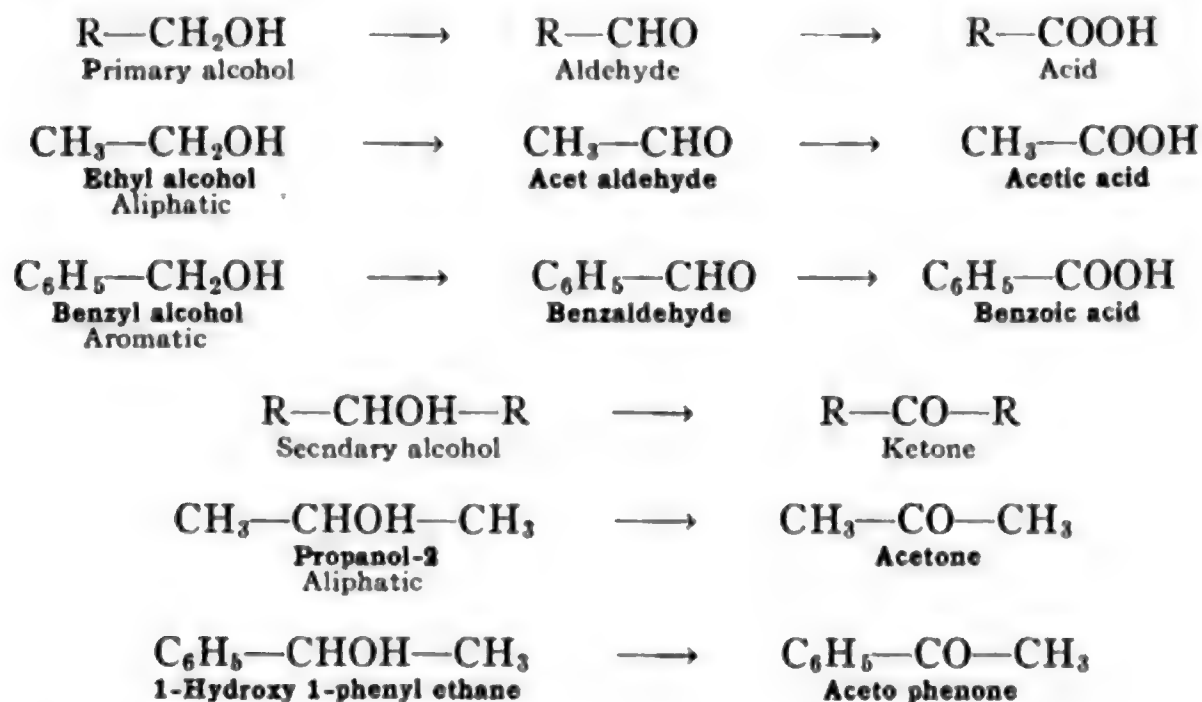
Both of these compounds yield sulphides or thio-ethers. Thio-phenol by the diazo reaction yields **di-phenyl sulphide**, $\text{C}_6\text{H}_5\text{—S—C}_6\text{H}_5$, **di-phenyl thio-ether** and benzyl mercaptan yields **di-benzyl sulphide**, $\text{C}_6\text{H}_5\text{—CH}_2\text{—S—CH}_2\text{—C}_6\text{H}_5$, **di-benzyl thio-ether**. These sulphides on oxidation yield *sulphones* (p. 526).



VIII. AROMATIC ALDEHYDES AND KETONES

In considering the aromatic aldehydes and ketones and later the aromatic acids it should be emphasized that the relationships discussed in Part I (p. 129) between alcohols, aldehydes, ketones and acids are general and apply just as truly to the aromatic compounds as to the aliphatic. The class characteristics of alcohols, aldehydes, ketones and acids are the same in both series. Thus the primary alcohols, on oxidation, always yield first aldehydes and then acids, while the secondary alcohols yield ketones.

General and specific formulas expressing these relationships are as follows:



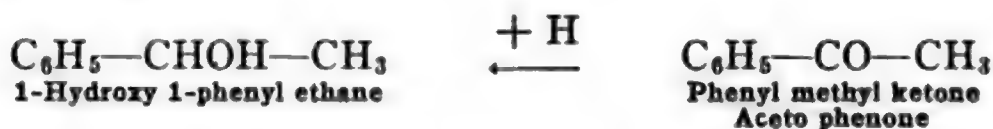
In aliphatic ketones we have both simple or symmetrical ketones, in which the two radicals (R) are alike, and mixed or unsymmetrical ketones, in which the two radicals are unlike. In aromatic ketones also, the two radicals may be alike and both aromatic, *e.g.*, $\text{C}_6\text{H}_5-\text{CO}-\text{C}_6\text{H}_5$, **di-phenyl ketone or benzophenone**, which is a symmetrical aromatic ketone. They may be unlike and both aromatic, *e.g.*, **phenyl tolyl**

ketone, $\text{C}_6\text{H}_5\text{—CO—C}_6\text{H}_4\text{—CH}_3$, which is unsymmetrical but wholly aromatic. Also one radical may be aromatic and the other aliphatic, *e.g.*, $\text{C}_6\text{H}_5\text{—CO—CH}_3$, **phenyl methyl ketone** or **aceto phenone**, which is a mixed aromatic-aliphatic ketone also unsymmetrical. This latter is the type of aromatic ketones related to the more common aromatic secondary alcohols.

Synthesis From Alcohols.—The general methods of synthesis of aromatic aldehydes and ketones are several. The aldehydes may be prepared by the direct oxidation of the corresponding primary alcohol, usually with dilute nitric acid, *e.g.*,



Conversely, as previously stated, the aldehydes on reduction yield the primary alcohols and in the case of benzaldehyde, which is a commonly occurring substance in oil of bitter almonds, this method is used in the preparation of the alcohol. In the case of the secondary alcohols oxidation to ketones is not easily accomplished but the reverse reaction, the reduction of the ketones to secondary alcohols does take place with ease.



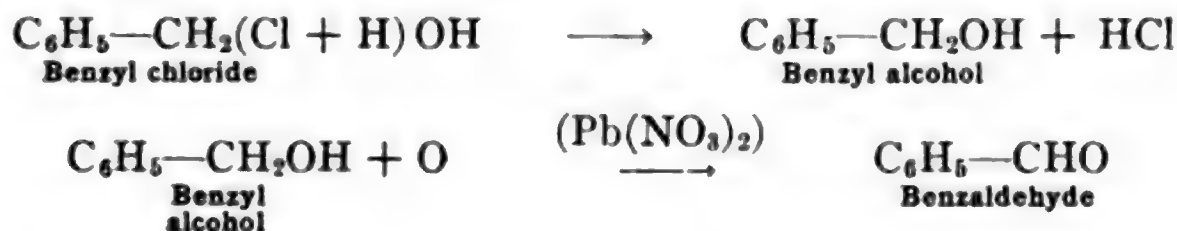
From Halogen Substitution Products.—Other common methods for the preparation of the aldehydes are those from the *halogen substitution products* of the benzene homologues where the halogen is substituted in the side-chain.

The di-halogen derivative of toluene of the class just mentioned, *viz.*, $\text{C}_6\text{H}_5\text{—CHCl}_2$, is known as **benzal chloride** because it yields **benzaldehyde** when boiled with water as follows:



In some cases this reaction takes place with water alone but usually some other substance is present; *e.g.*, calcium hydroxide or carbonate, potassium hydroxide, metallic iron or iron salts; which acts as a catalizer. The mono-chlorine derivative of toluene and other benzene homologues may also be used for preparing the aldehydes. In this case the reaction is in two steps, first, reaction with water yielding the alcohol, and second,

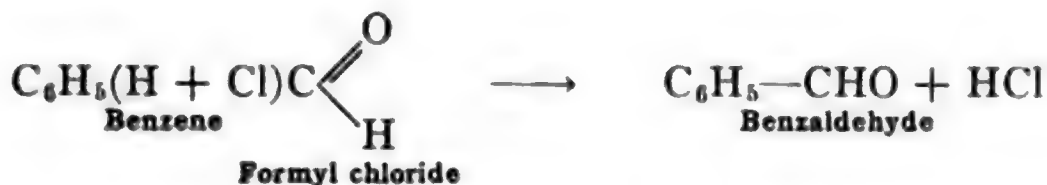
oxidation to the aldehyde. The reagent used is usually dilute nitric acid or a solution of lead nitrate.



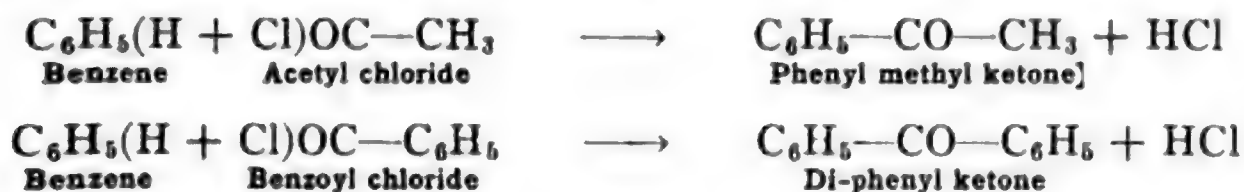
From Hydrocarbons.—An interesting method sometimes applicable for the preparation of aromatic aldehydes is from the hydrocarbons by means of the **Friedel-Craft** reaction, as modified by **Gattermann** and **Koch** with carbon monoxide and hydrochloric acid in the presence of CuCl . In this reaction formyl chloride, which is unknown in the free condition, is probably first formed by the union of the carbon monoxide and hydrochloric acid.



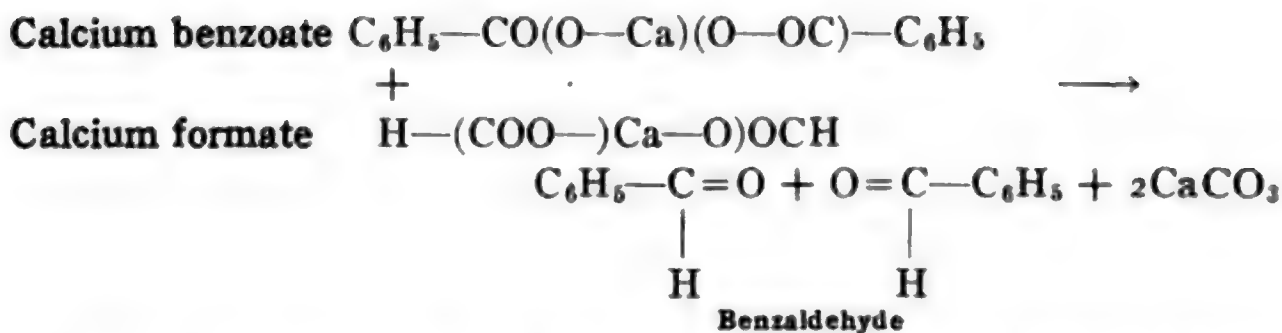
The hydrocarbon then reacts with the formyl chloride in the presence of CuCl as in the **Friedel-Craft** reaction with the elimination of hydrochloric acid as follows:



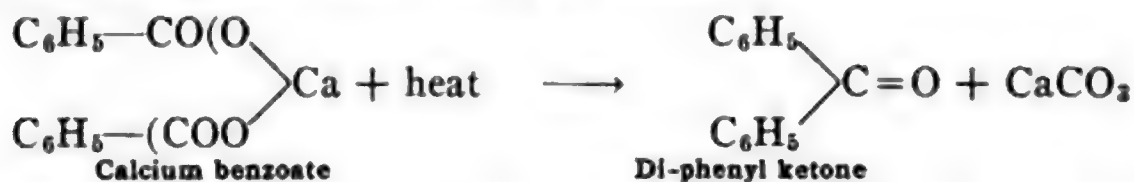
This method is applicable in preparing ketones if instead of formyl chloride ($\text{CO} + \text{HCl}$) an acid chloride is used as follows:



From acids.—A general method of synthesis of both aromatic aldehydes and ketones is from the calcium salts of acids. The reaction is of the same nature as that which takes place in the like synthesis of aliphatic aldehydes and ketones (Part I, p. 133). To obtain the aldehyde the calcium salt of formic acid is heated with the calcium salt of the aromatic acid.

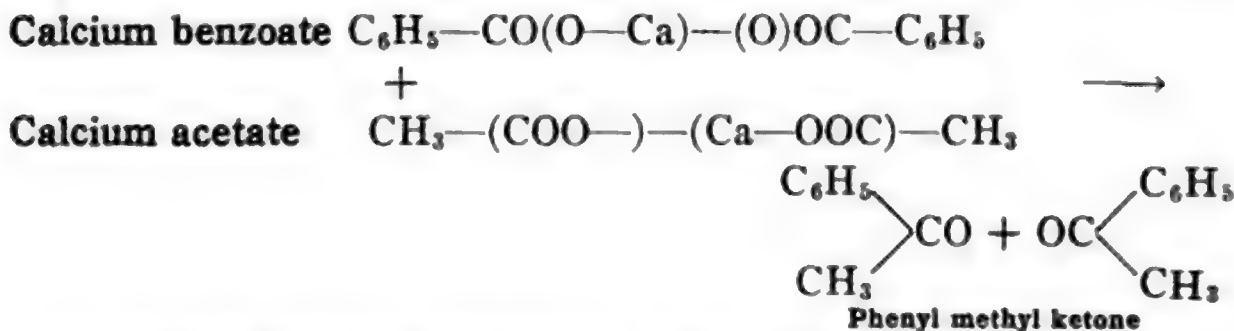


When the calcium salt of one aromatic acid alone is heated a symmetrical *di-aromatic ketone* results as follows:



The mixed calcium salts of two different aromatic acids will yield an unsymmetrical *di-aromatic ketone*.

If a mixture of the calcium salt of an aromatic acid and the calcium salt of an *aliphatic* acid is used the ketone resulting is a mixed *aromatic aliphatic* compound.



By this last reaction the product will not be a single compound but will consist of a mixture of phenyl methyl ketone, di-phenyl ketone and dimethyl ketone as both of the two preceding reactions take place.

Reactions.—The general properties and reactions of the aromatic aldehydes and ketones are like those of their aliphatic relatives. The aldehydes are easily oxidized to acids and reduce ammoniacal silver nitrate solution. Both aldehydes and ketones are easily reduced to alcohols. The aldehydes form addition products with sodium bisulphite and with hydrogen cyanide. With ammonia, however, they do not form addition products but react with the elimination of water and the formation of a condensation product which is a derivative of two molecules of ammonia.



The resulting compounds are known as hydramides and from benzaldehyde, as above, the compound formed is hydro benzamide.

Polymerization.—The characteristic property of aldehydes to polymerize (Part I, p. 117) is true of the aromatic aldehydes also but the reaction takes place in an entirely different manner than in the aliphatic series. When treated with potassium cyanide benzaldehyde polymerizes, or better, *condenses* as follows:



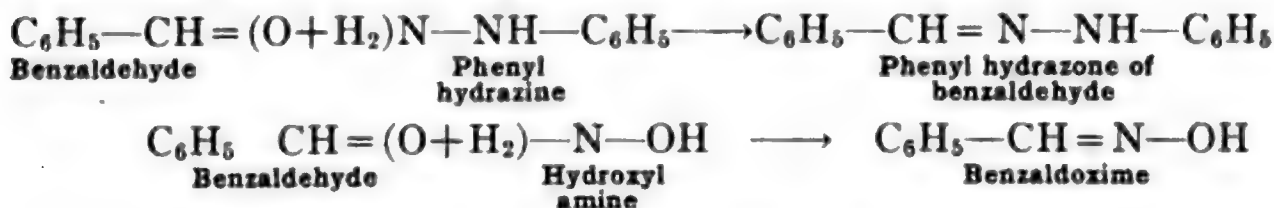
The compound formed is a mixed aromatic alcohol and ketone, *i.e.*, (hydroxy-methyl-phenyl) phenyl ketone, and is known as **benzoin**. This compound should properly be considered in the class of hydroxy ketones, which we shall take up a little later, but, because of its relation to benzaldehyde, it may also be mentioned here.

Oxidation of Ketones.—The aromatic ketones in which both an aromatic and aliphatic group are present undergo an important reaction when oxidized. Ordinarily ketones can not be oxidized without breaking down, because the carbon group containing the carbonyl oxygen has no remaining hydrogen atom united to it. In the case of an aromatic-aliphatic ketone, *e.g.*, $\text{C}_6\text{H}_5\text{—CO—CH}_3$, the oxidation consists in the conversion of the alkyl radical into carboxyl as follows:



The compound so formed is a mixed ketone acid and as such will be referred to again.

Oximes and Hydrazones.—The characteristic aldehyde and ketone reactions with **hydroxyl amine** and **phenyl hydrazine**, depending upon the carbonyl group, C=O , take place with the aromatic aldehydes and ketones just as they do with the aliphatic and yield *oximes* and *hydrazones*, the former being of especial importance.

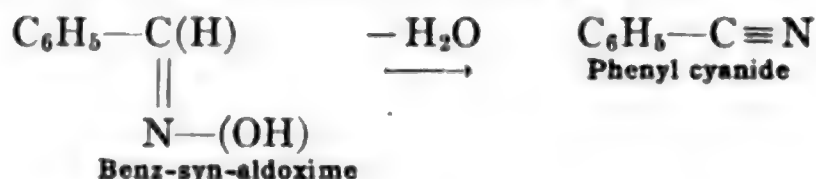


Isomerism of Benzaldoxime.—Benzaldoxime, the product of the last reaction, exhibits a very interesting case of *stereo-isomerism*. It exists in two forms which under certain conditions are readily trans-

formed into each other. This isomerism is *stereo-isomerism* of the **nitrogen atom** of the same nature as was found in the case of the *diazo compounds* (p. 592). The formulas expressing the isomeric forms are as follows:



The indication that the *syn* formula applies to that benzaldoxime which melts at 125° and not to the one which melts at 35°, is that the former readily loses water and is converted into **phenyl cyanide** or **benzoic nitrile**. This will be clearly seen as follows:



The *anti* form, with the hydroxyl and the hydrogen on opposite sides, would not thus easily lose water, and in fact it does not.

The naming of the isomeric aldoximes follows the same plan as in the case of the diazo compounds (p. 592), the prefixes *syn* and *anti* being used. The prefix *syn* means that the hydroxyl group is on the *same side* of the doubly linked nitrogen and carbon atoms as some other group while *anti* indicates that the two are on opposite sides. In the diazo compounds the phenyl or other benzene group is the only other group present and the terms *syn* and *anti* refer to the relation of the hydroxyl group to this benzene group.

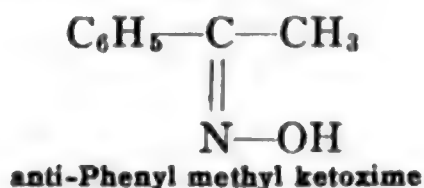
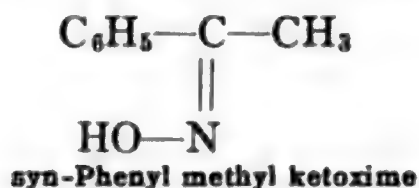


In the oximes of the aromatic aldehydes and ketones, however, *two* other groups are present and the names must indicate to which of these groups the *syn* or *anti* relationship of the hydroxyl group applies.

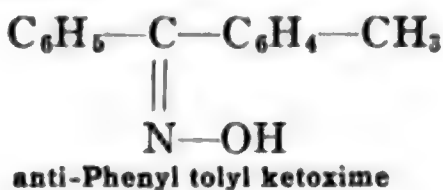
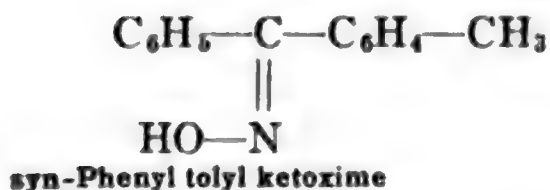


The prefix is placed immediately before the name of the group concerned, *i.e.*, *syn-aldoxime* means that the aldehyde hydrogen atom is *syn* to the hydroxyl group and *anti-aldoxime*, that the aldehyde group is *anti* to the hydroxyl group. If the prefixes referred to the benzene group the names would be reversed and benz-*syn*-aldoxime would be anti-benzaldoxime and benz-*anti*-aldoxime would be *syn*-benzal-doxime. These last names, however, are *not used*.

Isomerism of Ketoximes.—In the case of aromatic *aldehydes* they all yield these stereo-isomeric oximes. With the aromatic *ketones* the condition is different and some yield stereo-isomers and some do not. With symmetrical aromatic ketones in which the two radicals are *alike*, such as **di-phenyl ketone**, $\text{C}_6\text{H}_5\text{—CO—C}_6\text{H}_5$, no different space relation of the hydroxyl group is possible as the two forms will be identical. When, however, the ketone is unsymmetrical, *i.e.*, the two radicals are *unlike*, as in mixed aromatic-aliphatic ketones such as **phenyl methyl ketone**, $\text{C}_6\text{H}_5\text{—CO—CH}_3$, or in unsymmetrical di-aryl ketones such as **phenyl tolyl ketone**, $\text{C}_6\text{H}_5\text{—CO—C}_6\text{H}_4\text{—CH}_3$, then the two stereo forms are possible though both forms are not known in all cases.

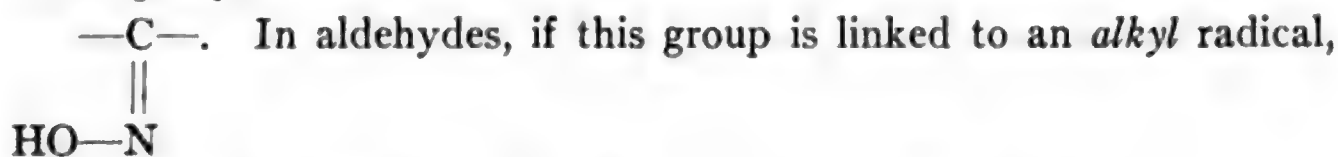


(only one known)

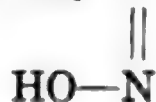


(both known)

As just stated the two possible stereo-isomers are not always known. The stability and possible isolation of the two forms seems to be connected with the linkage of *benzene rings* or *alkyl radicals* to the *carbo-oxime group*,



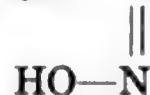
as in **acetaldoxime**, $\text{CH}_3\text{—C—H}$, or in **phenyl acet aldoxime**,



$\text{C}_6\text{H}_5\text{—CH}_2\text{—C—H}$, only *one* form is known. Similarly in the ket-

$$\begin{array}{c} \text{C}_6\text{H}_5\text{—CH}_2\text{—C—H} \\ \parallel \\ \text{HO—N} \end{array}$$

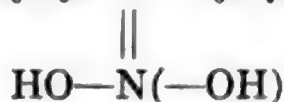
oximes if this carbo-oxime group has *one alkyl* radical linked to it only *one* form is known, as in **phenyl methyl ketoxime**, $\text{C}_6\text{H}_5\text{—C—CH}_3$, (see



above). On the other hand unsymmetrical di-aryl ketoximes in which two benzene rings are linked to the carbo-oxime group are known in the two forms as in **phenyl tolyl ketoxime**, $\text{C}_6\text{H}_5\text{—C—C}_6\text{H}_4\text{—CH}_3$ or in

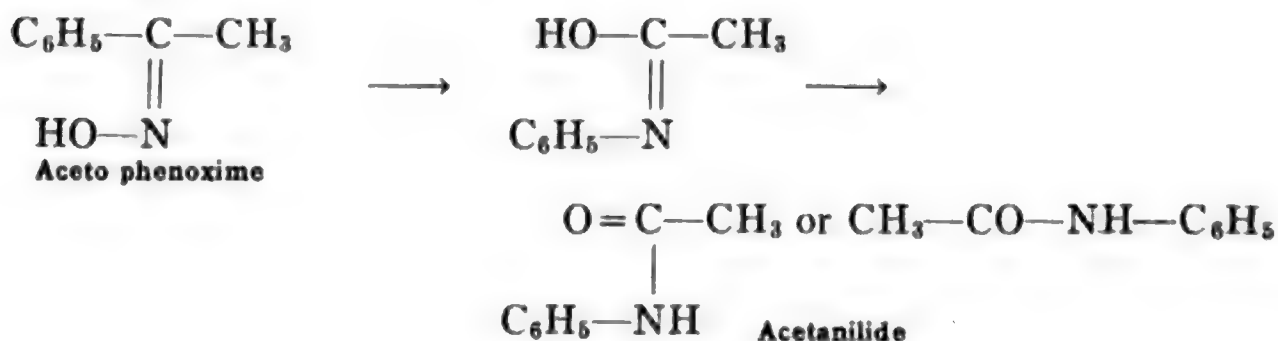


phenyl chlor-phenyl ketoxime, $\text{C}_6\text{H}_5\text{—C—C}_6\text{H}_4\text{Cl}$.



The fact that only one form is known, when the two are possible, may be due to extreme instability; one form readily changing over to the other, so that only one is isolated. That the known compound, in those cases where only one has ever been isolated, is in fact one of these stereo forms, probably the *syn* form, is indicated by the decomposition products and by a study of a transformation known as the **Beckmann rearrangement**.

Beckmann Rearrangement.—When **phenyl methyl ketoxime**, **acetophenoxime**, is treated with acid chlorides or phosphorus penta-chloride, it is converted into **acetanilide**. The steps in the reaction are as follows:

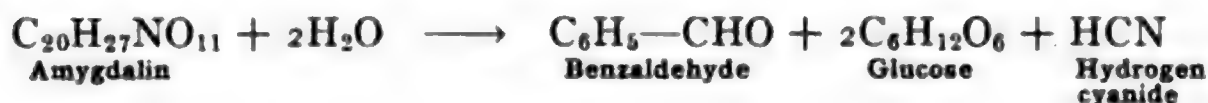


A. ALDEHYDES

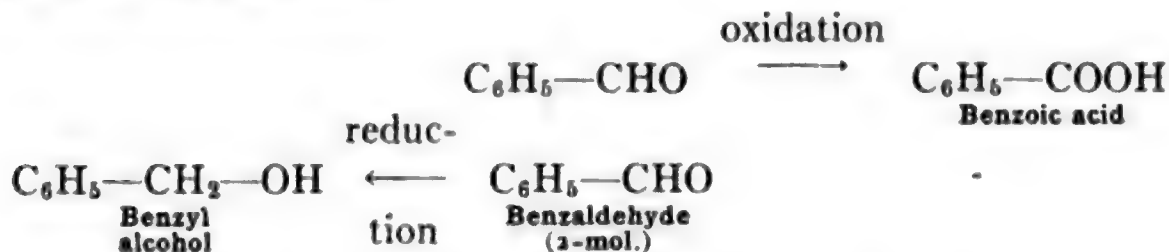
Benzaldehyde, $\text{C}_6\text{H}_5\text{—CHO}$

Amygdalin.—**Benzaldehyde**, the simplest of the aromatic aldehydes, occurs in nature as a constituent part of the glucoside **amygdalin**, in

bitter almonds, in the kernels of peach stones and in some other plants. The glucoside consists of **benzaldehyde**, **glucose** and **hydrocyanic acid** in combination. When this undergoes hydrolysis these three constituents are obtained as the products. In almonds there is also present an enzyme known as **emulsin** which possesses the property of effecting this hydrolysis. Therefore when bitter almonds are ground and mixed with cold water, enzymatic hydrolysis of the glucoside occurs and one of the products is benzaldehyde. Hence the aldehyde is commonly known as **oil of bitter almonds**. The reaction which takes place in the hydrolysis of amygdalin is as follows:



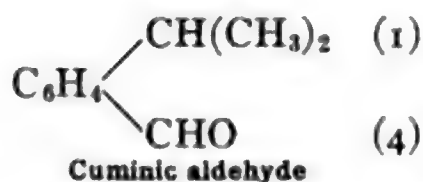
Benzaldehyde is a colorless liquid when pure, m.p. -13.5° , b.p. 180° . It has a strong odor of the natural oil of bitter almonds and is used as a flavoring substance and in perfumery. Because of its easy preparation and common occurrence it has been thoroughly studied and the reactions which it undergoes have been well established. It will be recalled that one of the classic joint researches of **Liebig** and **Wöhler**, and one which did much for the establishment of the radical theory, was: "**Concerning The Radical of Benzoic Acid.**" It was their study of oil of bitter almonds which led them to this investigation published in 1832 (p. 14). The aldehyde is easily oxidized, even in the air, to benzoic acid, hence its name **benzoic aldehyde** or **benzaldehyde**. This oxidation also occurs with the simultaneous reduction to **benzyl alcohol** so that when it is treated with strong potassium hydroxide it is converted partly into one compound and partly into the other. That is, two molecules act together, one being reduced or oxidized at the expense of the other.



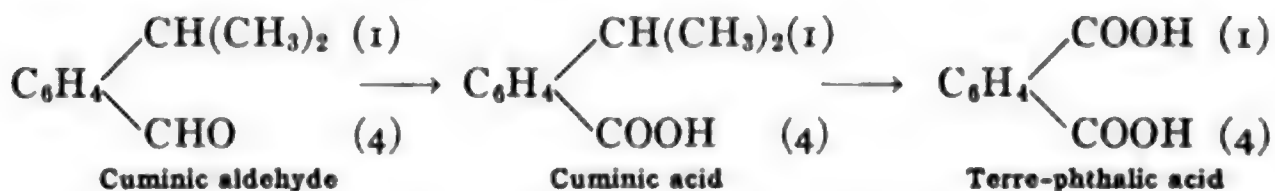
In its general reactions it is like all aldehydes. It is an important reagent in all cases where an aldehyde is needed and in the manufacture of certain dyes, *e.g.*, **malachite green** (p. 747).

Higher Aromatic Aldehydes

Cuminic Aldehyde.—Only two of the higher aldehydes are of sufficient importance to require mention, viz., **cuminic aldehyde** and **cinnamic aldehyde**. The first is the aldehyde of **iso-propyl benzene** with the aldehyde group in the *para* position.



It is known as cuminic aldehyde because of its occurrence in *Roman oil of cumin*. It oxidizes to an aromatic acid known as **cuminic acid** which is **para iso-propyl benzoic acid**. On further oxidation the aliphatic side chain is likewise oxidized to carboxyl and a di-basic acid, **terrephthalic acid**, results. This acid is obtained by the complete oxidation of **para-xylene** and hence is a *para* compound. This establishes cuminic aldehyde as a *para* compound also.



Cinnamic Aldehyde.—The other aromatic aldehyde which we shall mention is **cinnamic aldehyde**. It contains the aldehyde group in the side chain and not in the benzene ring, and is thus an aliphatic aldehyde substitution product of benzene. The aliphatic side chain is also an unsaturated chain. Its formula is $\text{C}_6\text{H}_5\text{—CH=CH—CHO}$, and it may be considered as **beta-phenyl acrylic aldehyde**. As an aldehyde it yields by oxidation an acid, viz., **beta-phenyl acrylic acid** or, as it is commonly known, **cinnamic acid**. The aldehyde is found in *oil of cinnamon* obtained from cinnamon bark, hence its name and the name of the acid. The most important synthesis is by the condensation of **benzaldehyde** and **acetaldehyde**, as follows:



Cinnamic aldehyde reacts as benzaldehyde does and is important as a synthetic reagent in the same classes of reactions.

B. KETONES

Aceto Phenone, $C_6H_5-CO-CH_3$, Phenyl Methyl Ketone

Only two individual ketones will be mentioned in detail and they have already been repeatedly referred to in the preceding discussion of general facts. They are,

$C_6H_5-CO-CH_3$, **Phenyl methyl ketone** or **Aceto phenone**.

and $C_6H_5-CO-C_6H_5$, **Di-phenyl ketone** or **Benzo phenone**.

Aceto phenone is the simplest of the aromatic ketones related to secondary aromatic alcohols. It is a crystalline substance; m.p. 20.5° , b.p. 202° . It possesses a soporific or hypnotic effect on account of which it is also known as *hypnone*. Its reactions are those already considered. The oxime produced by the action of hydroxyl amine would seem to be possible of existence in two stereo-isomeric forms like the **benzaldoximes** as the two radicals joined to the carbo-oxime group are different. In fact only one oxime is known as has been explained.

$C_6H_5-C-CH_3$ **syn-Phenyl methyl ketoxime**

||
HO—N (anti-Aceto phenoxime)

The proofs that the known form is the *syn* compound are that it does not break up and yield **phenyl cyanide** and that it yields **acet anilide** by the **Beckmann rearrangement** which has just been discussed (p. 654).

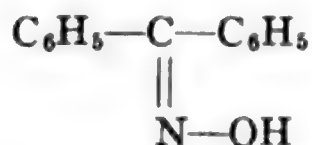
Benzo Phenone, $C_6H_5-CO-C_6H_5$, Di-phenyl Ketone

Benzo phenone is a solid which is di-morphous, *i.e.*, it exists in two forms which are not isomeric as they possess the same formula in every respect. One form is a solid, m.p. 26° , while the other is a solid, m.p. 46° . On reduction with zinc dust benzo phenone yields first the corresponding secondary alcohol, $C_6H_5-CH(OH)-C_6H_5$, and then the hydrocarbon **di-phenyl methane**, $C_6H_5-CH_2-C_6H_5$.

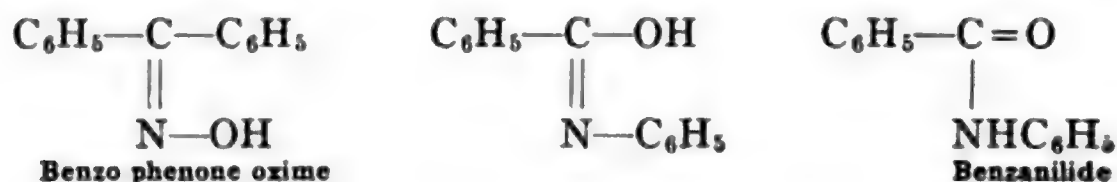


This hydrocarbon, **di-phenyl methane**, is a member of another series which will be considered later and, strictly speaking, benzo phenone does not belong to the group of aromatic ketones which we have been studying. Because of its close analogy to the other aromatic ketones

it seems best, however, to take it up at this time. Benzo phenone being symmetrical in constitution yields only one oxime,



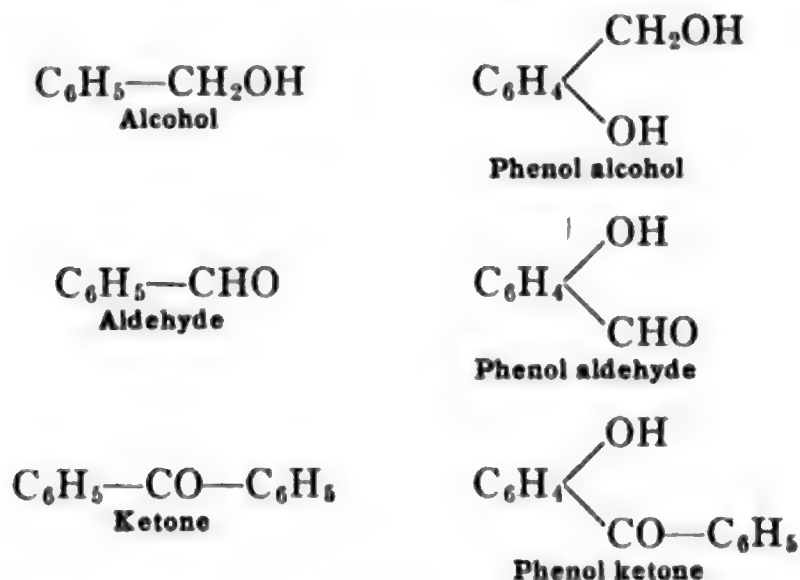
This oxime, however, undergoes the **Beckmann rearrangement** and yields **benzanilide** just as **aceto phen-oxime** yields **acet anilide**.



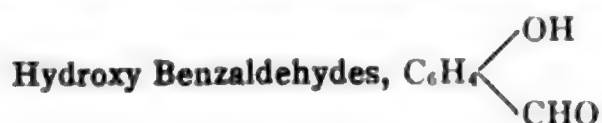
SUBSTITUTED ALDEHYDES AND KETONES

HYDROXY ALDEHYDES AND HYDROXY KETONES

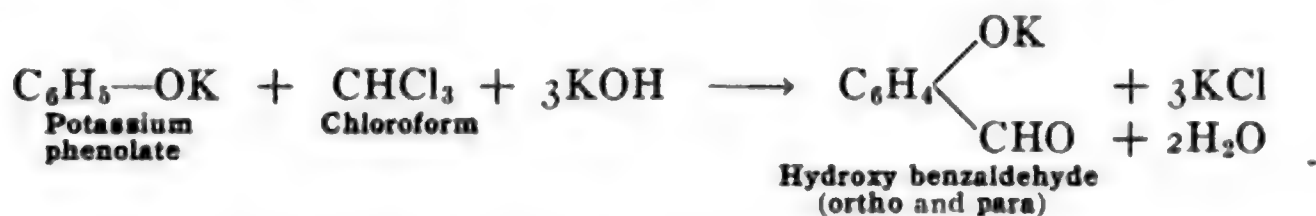
Phenol Aldehydes and Ketones.—The most important substitution products of aromatic aldehydes and ketones are those containing the hydroxyl group. Analogous to the phenol alcohols we have the *phenol aldehydes* and *phenol ketones* which are ring hydroxy substitution products of the aromatic aldehydes and ketones.



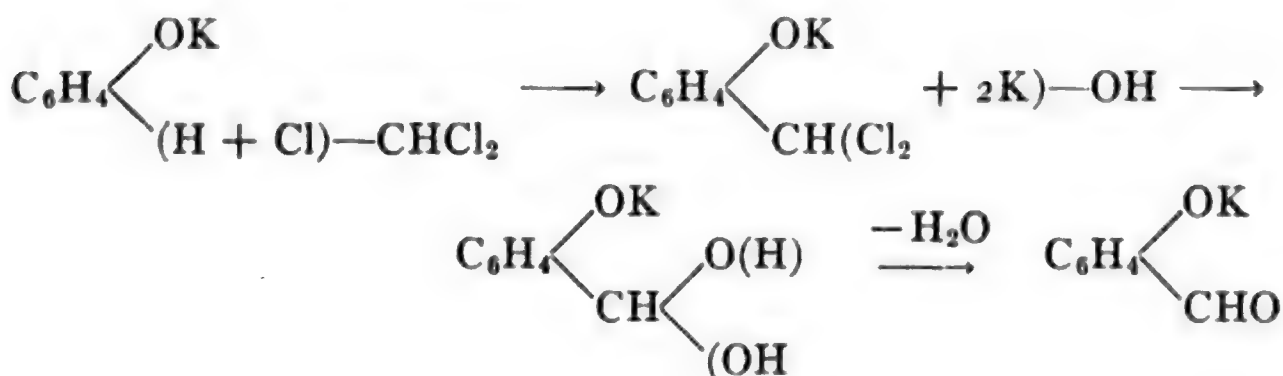
Some members of this class of compounds and especially some of their ether derivatives are very valuable natural products.



Reimer-Tiemann Reaction.—Both the *ortho*- and *para*-hydroxy benzaldehydes are important. They may both be synthesized by what is known as the **Reimer-Tiemann reaction**. This consists of the interaction between a salt of a phenol and chloroform in the presence of an excess of alkali. The result is the introduction of the aldehyde group, ($-\text{CHO}$), into the benzene ring of the phenol as follows:

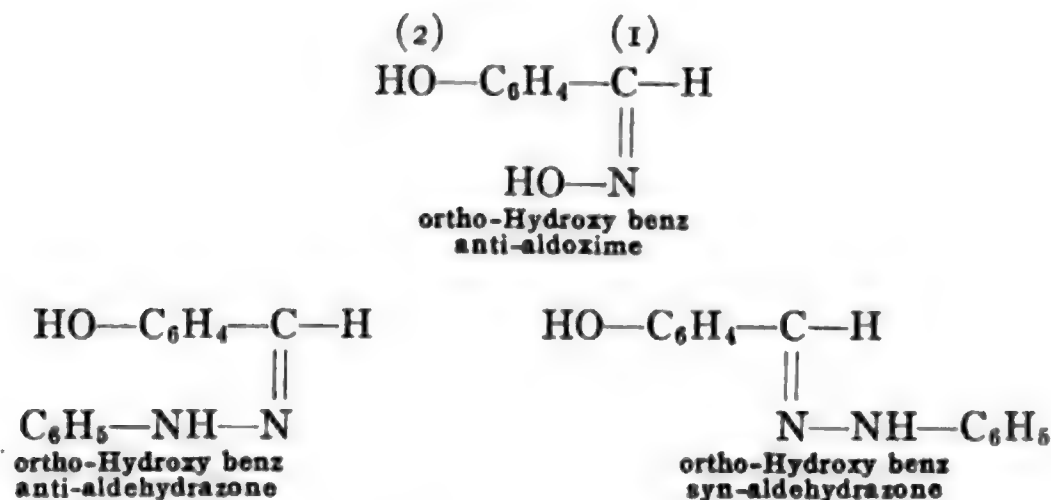


The reaction probably takes place by the following steps:

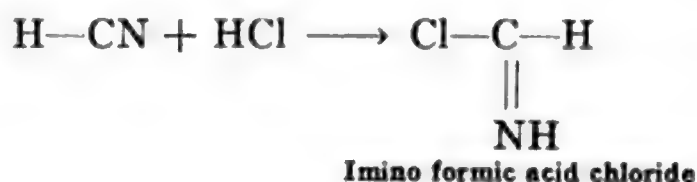


The reaction is a general one for phenols both *mono*- and *poly*-, and for the ethers of poly-phenols. It results always in a mixture of the *ortho* and *para* compounds. In the preparation of hydroxy benzaldehyde the two may be easily separated as the *ortho* compound is volatile with steam, while the *para* compound is not.

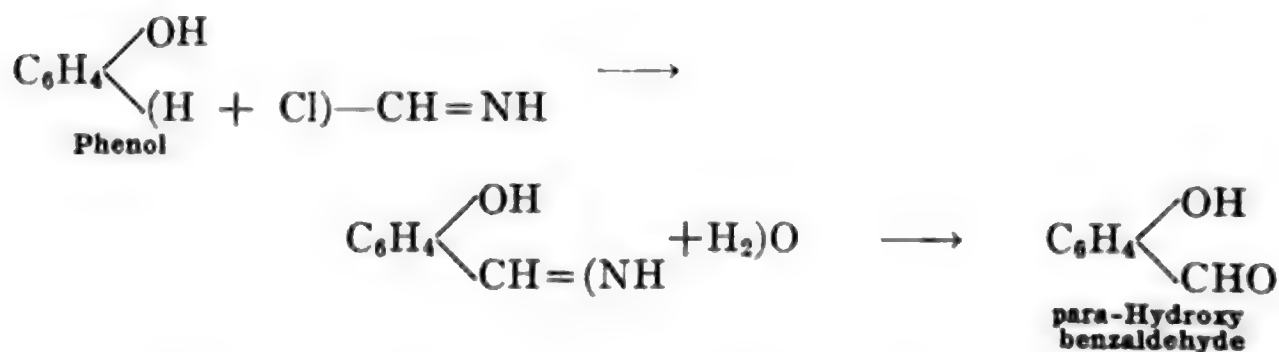
Salicylic Aldehyde.—The *ortho*-hydroxy benzaldehyde is also known as **salicylic aldehyde** because on oxidation it yields **salicylic acid**, *ortho*-hydroxy benzoic acid. It may also be made by oxidizing *ortho*-hydroxy benzyl alcohol, salicylic alcohol (p. 646), or by oxidizing the glucoside **salicin** from which the alcohol is obtained on hydrolysis. It occurs naturally in the oil of the flowers, leaves and stems of certain spiraea plants. It is an oil with a characteristic odor. At -20° it solidifies to large crystals and it boils at 196.5° . It is slightly soluble in water and gives a violet color with ferric chloride. It reduces **Fehling's** solution and forms a crystalline addition compound with sodium acid sulphite like aldehydes in general. It yields an oxime and a hydrazone, the former known in *one* stereo form, the latter in *two*.



***para*-Hydroxy Benzaldehyde.**—Besides being formed together with the *ortho* compound by the **Reimer-Tiemann reaction** the ***para* hydroxy benzaldehyde** may be synthesized from phenol by a modification of the **Gattermann-Koch reaction** (p. 649), for introducing the aldehyde group into a benzene ring. In this synthesis hydrogen cyanide and hydrochloric acid, together with aluminium chloride, are used. The first two react similarly to carbon monoxide and hydrochloride acid (p. 649) and give the chloride of **imino formic acid**.



In the presence of aluminium chloride this compound reacts with phenol yielding an *ald-imide* which with water gives the hydroxy aldehyde.



The advantage of this synthesis is that the *para* compound only is formed and that phenol ethers undergo the reaction also. The ***para*-hydroxy benzaldehyde** is not volatile with steam, is quite soluble in

water and gives only a slight violet color with ferric chloride. It forms an addition product with sodium acid sulphite and an oxime and hydrazones with hydroxyl amine and phenyl hydrazine.

Ethers. Essential Oils

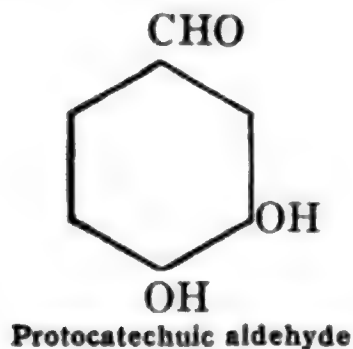
The ether derivatives of the phenol aldehydes like the ether derivatives of the phenols themselves are important as constituents of essential oils present in many plants.

Anis Aldehyde.—The simplest essential oil constituent of this group is one found in *anis seed oil* and known as **anis aldehyde**.

It is the **methyl ether of para-hydroxy benzaldehyde**, $C_6H_4 \begin{matrix} \swarrow OCH_3 \\ \searrow CHO \end{matrix}$.

It is a liquid, m.p. -4° , b.p. 245° , with a pleasant odor of white thorne flowers and is used in perfumes. It is interesting that while hydroxy benzaldehyde itself yields only one form of oxime the anis aldehyde yields the two stereo-isomeric forms. This is attributed to the influence of the free hydroxyl group in preventing the formation of isomers. In the anis aldehyde the hydroxyl group is converted into methoxy and the isomers are obtained.

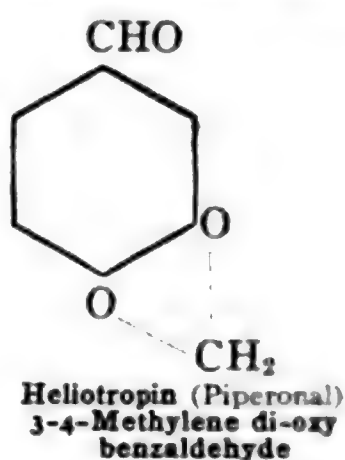
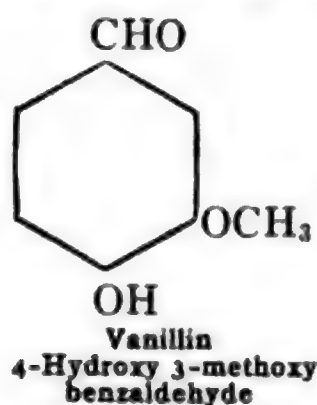
Protocatechuic Aldehyde.—A *di-phenol* aldehyde, viz., the **3-4-di-hydroxy benzaldehyde**, is known as **protocatechuic aldehyde** because it yields **protocatechuic acid** on oxidation.



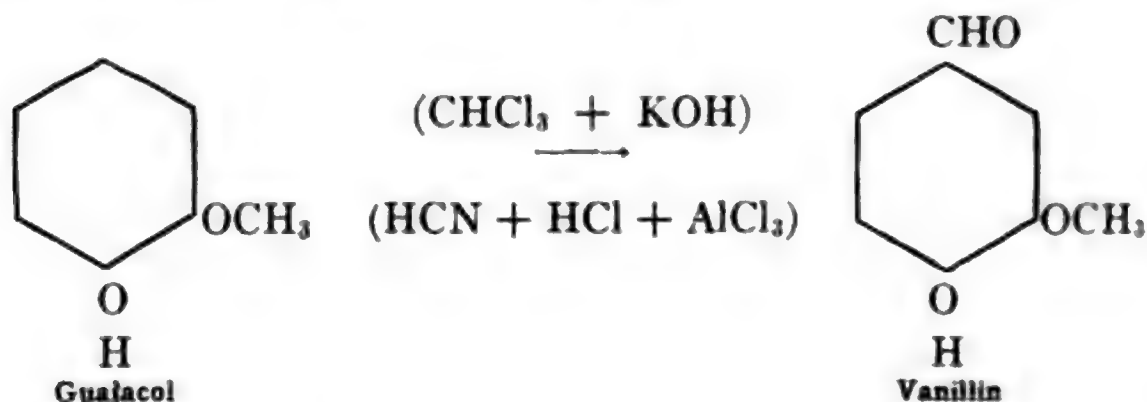
It may be synthesized by the **Reimer-Tiemann** or **Gattermann-Koch** reactions from **pyrocatechinol**, **1-2-di-hydroxy benzene**.

Vanillin.—Two very important essential oil constituents are ether derivatives. One of these is **vanillin**, the chief constituent of *vanilla beans* from which *vanilla extract* is made, and the other is **heliotropin**, also known as **piperal**, which has the odor of *heliotrope flowers*. **Vanillin** is the **mono-methyl ether of protocatechuic aldehyde**, the methoxy

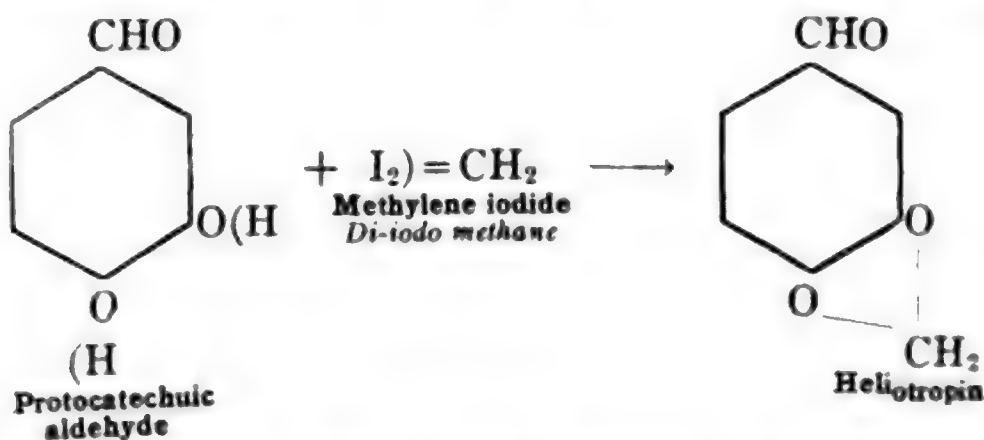
group being in the *meta* position to the aldehyde group. **Heliotropin** is the methylene di-ether of the same aldehyde. The formulas are,



Just as protocatechuic aldehyde may be synthesized by the **Reimer-Tiemann** or **Gattermann-Koch** reactions from the di-phenol **pyrocatechinol**, so vanillin may be made by the same reactions from the mono-methyl ether of pyrocatechinol, *i.e.*, **guaiacol** (p. 621).

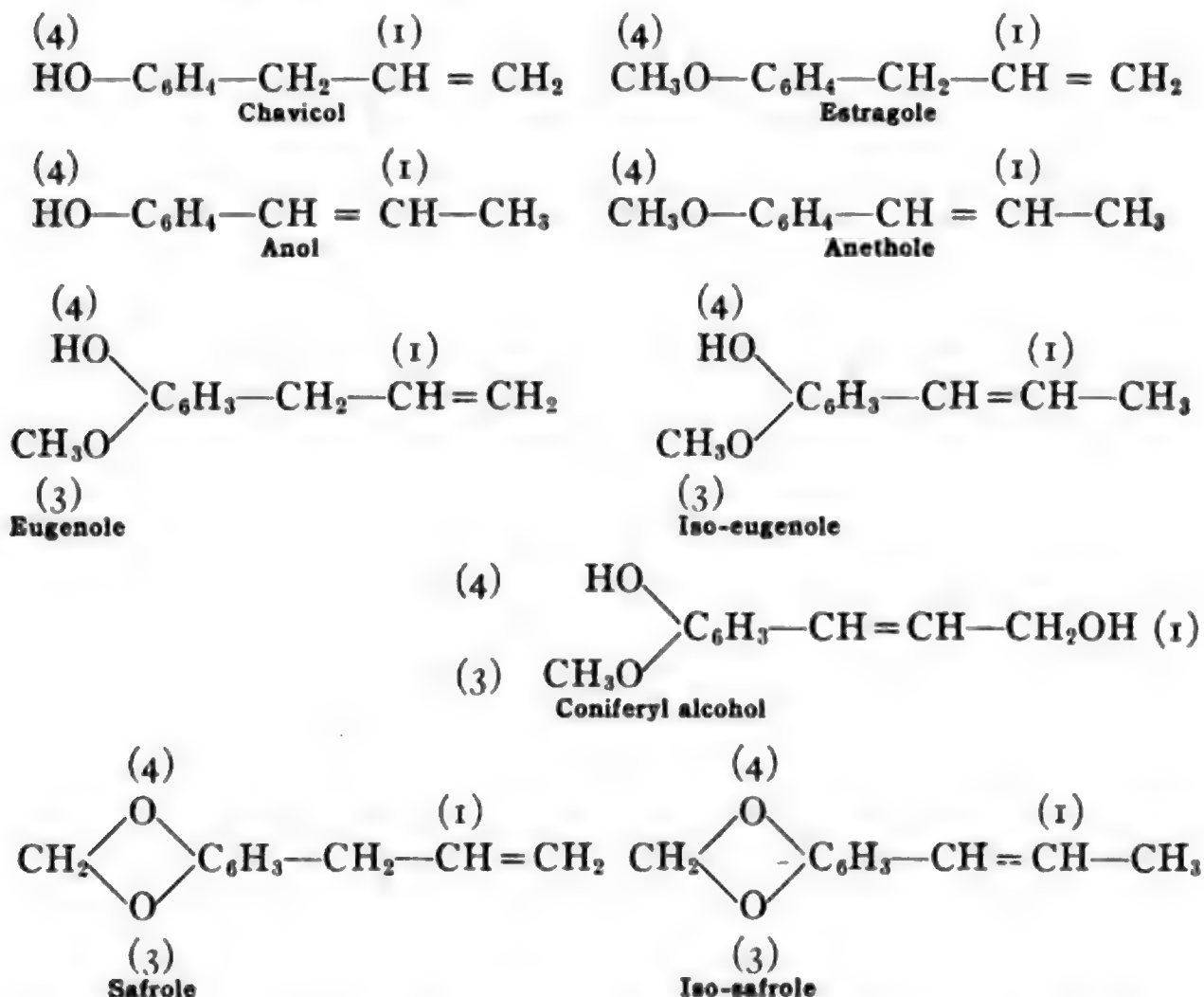


Heliotropin may be prepared from protocatechuic aldehyde by the action of **methylene iodide**, CH_2I_2 , the yield, however, being small.



Relation to Eugenole, etc.—By far the most important syntheses of these important essential oil constituents are by the oxidation of the corresponding ethers of di-hydroxyl derivatives of benzene homologues

which contain an *unsaturated side chain*. All of these compounds are important essential oil constituents and the syntheses referred to have been the means of showing the relationship between them. We have previously discussed the methyl and methylene ethers of the mono- and di-phenols with unsaturated side chain (p. 623). Their formulas may be repeated as follows:

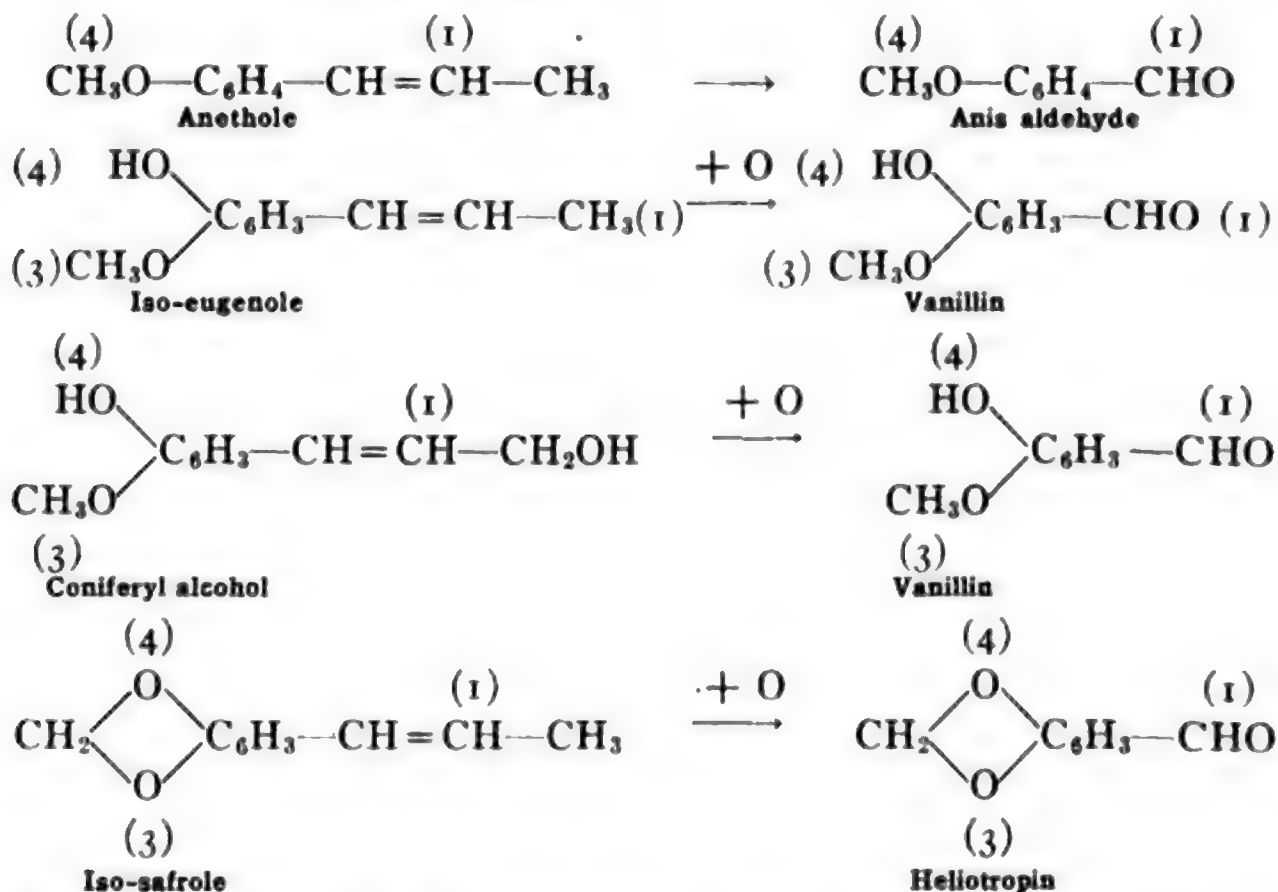


It will be recalled that the difference between **eugenole** and **safrole** on the one hand and the corresponding *iso* compounds, **iso-eugenole** and **iso-safrole**, on the other is, that in the latter and also in **coniferyl alcohol**, **anol** and **anethole**, the benzene ring is in the *alpha* or 1 position in the unsaturated propene or propenol chain. When such an unsaturated side chain compound is oxidized the chain breaks at the double bond and yields the aldehyde of the benzene compound.



The following reactions and relationships have thus been established, and they have become the chief synthetic methods used in the prepara-

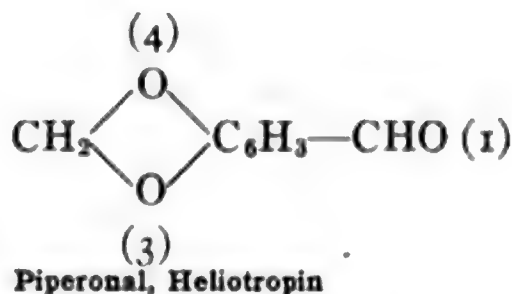
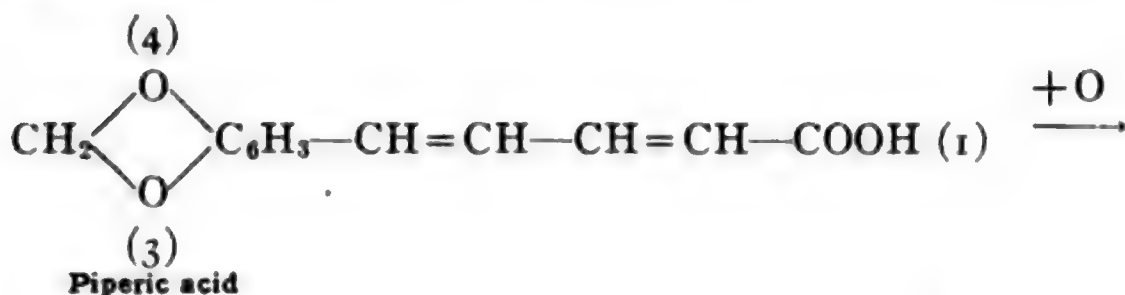
tion of these valuable compounds. The iso-compounds, being readily prepared from their isomers, either set of compounds may thus be used as a source of the preparation.



Vanillin is present in the vanilla bean to the amount of about 2.0 per cent, accumulating as white crystalline needles. It is also found in smaller amounts in several other plants and plant resins or balsams, *e.g.*, gum benzoin, Peru balsam, Tolu balsam, *Orchideae nigretella*, etc. It crystallizes in white needles, m.p. 80°, b.p. 285°, soluble in 90–100 parts cold water and 20 parts of hot. It possesses the characteristic odor and flavor of the common vanilla extract. It is now prepared in considerable commercial quantities by one of the above synthetic methods mostly from **eugenole** which yields first **iso-eugenole**; or from the glucoside **coniferin**, which yields **coniferyl alcohol**. It is interesting that the synthetic vanillin can be used in all cases in place of the natural vanilla extract when the object is odor, as in perfumes, the aroma being similar but weaker. When it is used as a flavor the synthetic product can only partially replace the natural. This is due to the fact that in the synthetic product it is very difficult to remove all traces of the by-products. Pure vanillin costs about \$50 to \$60 per pound. A water solution of vanillin acts weakly acid and is colored by ferric chloride a slight

blue-violet. It yields characteristic oximes and hydrazones. When heated with hydrochloric acid it hydrolyzes to protocatechuic aldehyde, and when fused with potassium hydroxide it yields the corresponding di-hydroxy acid.

Heliotropin, Piperonal.—**Heliotropin** receives its other name of **piperonal** from its relation to compounds occurring in *pepper*. In black pepper, *Piperus nigra*, there is present an alkaloid known as **piperine** (p. 888). From this alkaloid an acid, piperic acid, is obtained. This acid is a methylene di-ether containing an alpha unsaturated side chain as in **iso-eugenole**, etc. On oxidation the side chain breaks at the double bond, as has been explained, and yields an aldehyde which is **piperonal**.



Heliotropin is prepared commercially by the synthesis given above from safrole through iso-safrole. It is used in perfumes on account of its very pleasant odor of heliotrope flowers. It forms crystals, m.p. 37°, b.p. 263°. By boiling with water it hydrolyzes and yields protocatechuic aldehyde just as vanillin does. It also yields oximes and hydrazones which are characteristic.

Alcohol-aldehydes and -ketones.—If the hydroxyl group in hydroxy aldehydes and ketones is in the side chain instead of the ring then the compounds instead of being mixed phenol-aldehydes will be *alcohol-aldehydes* or *-ketones*, e.g.,



Phenyl tetrose
2-3-4-Tri-hydroxy 4-phenyl butyric aldehyde



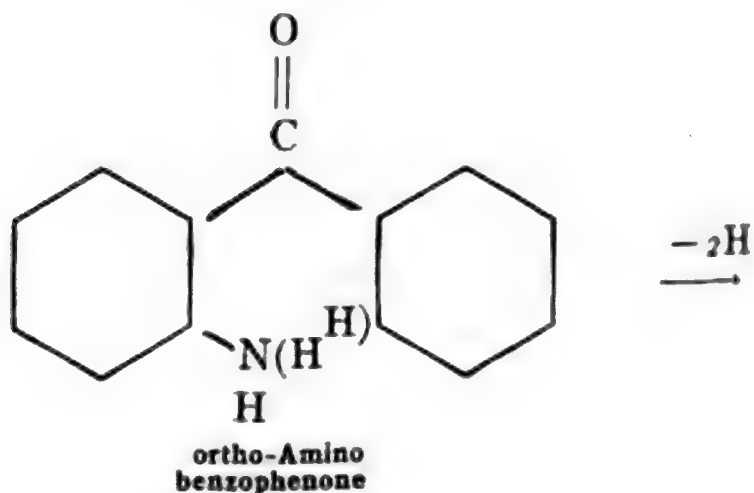
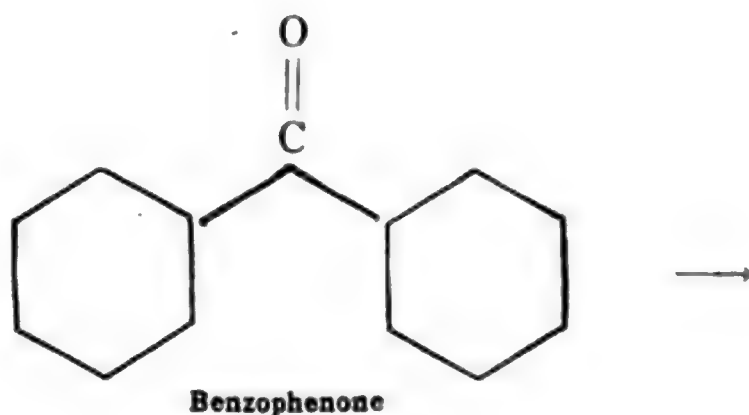
Hydroxy aceto phenone

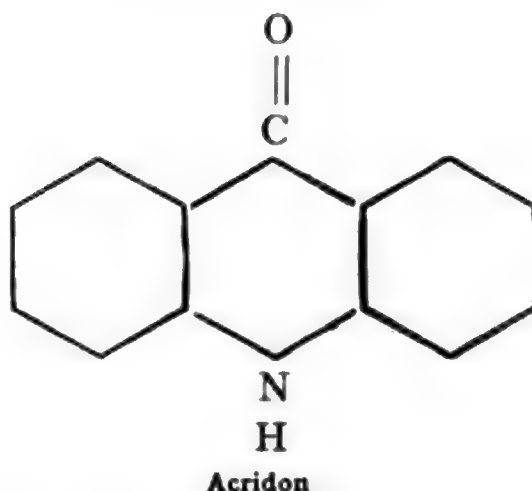
Such compounds, if they contain more than two hydroxyl carbon groups in the saturated side chain, are plainly phenyl derivatives of the sugars as in the first formula above.

AMINO KETONES

Nitro and amino substituted aromatic aldehydes and ketones are not of special importance except in two cases that may be cited.

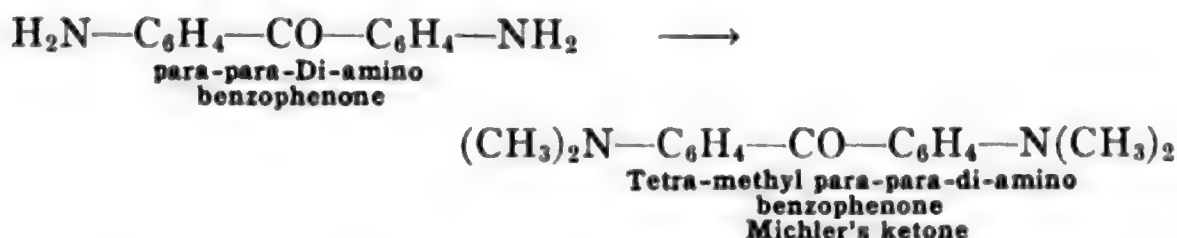
ortho-Amino Benzophenone.—Benzophenone yields an *ortho-nitro* substitution product with the nitro group substituted in one of the benzene rings in the position ortho to the carbonyl group. This nitro compound by reduction, like all nitro compounds, yields the corresponding amino compound. When this **ortho-amino benzophenone** is oxidized two hydrogens are lost, one from the amino group and the other from the benzene ring which is not joined to nitrogen, and the two groups become united. This results in a compound in which two benzene rings are doubly linked to each other on one hand by the *carbonyl group* of the original benzophenone and on the other by the *imino group* as follows:



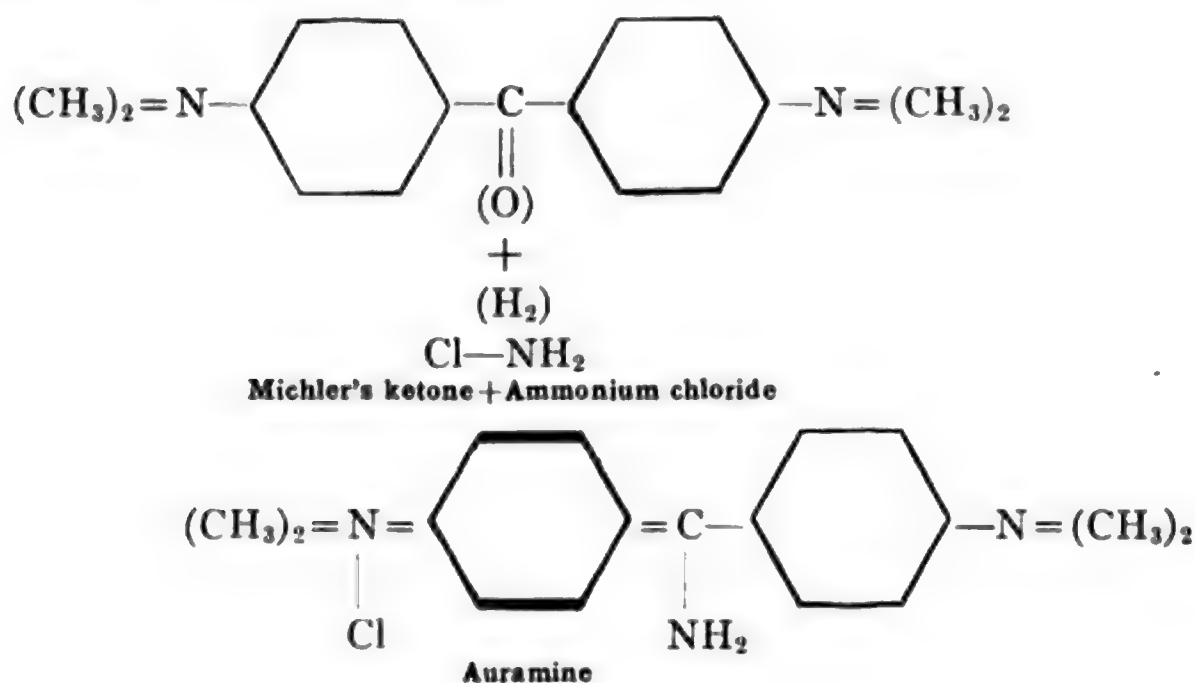


The compound formed is known as acridon.

Michler's Ketone.—A similar di-amino compound in which two amino groups are substituted in benzophenone in the para position in each of the benzene rings yields a tetra-methyl amino product which is known as **Michler's ketone**.



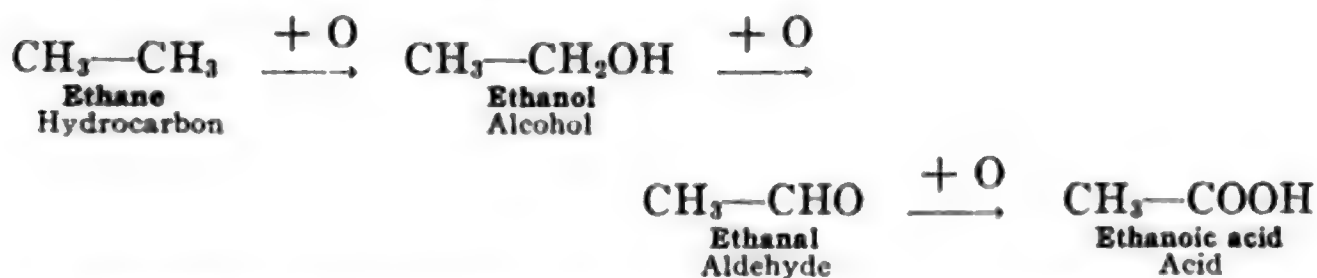
Auramine.—When this **Michler's ketone** is treated with ammonium chloride water is lost and a compound is formed of the constitution shown in the following reaction:



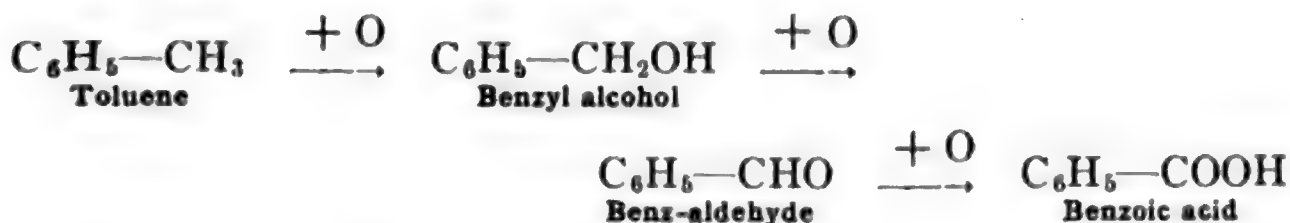
In this compound one of the amino nitrogens becomes penta-valent as in ammonium salts while the other remains tri-valent. The benzene ring to which the penta-valent nitrogen is linked takes on the *quinoid* structure as in *quinone*, while the other benzene ring retains its normal ring structure. The compound which is formed is known as **auramine**, and is the mother substance of important dyes. As will be mentioned, in connection with dyes, the presence of a quinoid group is associated with the dye character of compounds.

IX. AROMATIC ACIDS

Character and Types.—Aromatic acids bear exactly the same relationship to aromatic primary alcohols and aldehydes that the aliphatic acids do to the aliphatic primary alcohols and aldehydes, *i.e.*, the acids are the final oxidation products of the other two groups. In the aliphatic series we showed how the alcohols may be considered as the first oxidation products of the hydrocarbons. The entire series of oxidation relationships being illustrated as follows:

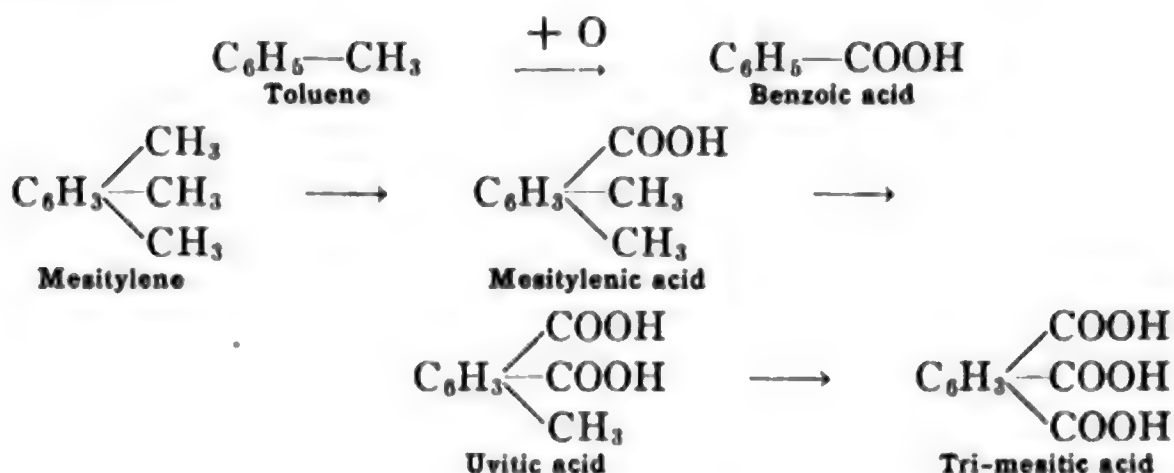


Methyl to Carboxyl.—In other words the acid group —COOH, *carboxyl*, is the complete oxidation product of the *methyl group*. In the aliphatic series the first step; methyl group to primary alcohol group, (—CH₃)→(—CH₂OH), and also the complete oxidation, methyl group to carboxyl group, (—CH₃)→(—COOH); has never been accomplished as a laboratory process. However, the other steps have been, and the relationship is accepted as practically established. The acceptance of it as a true relationship has been strengthened by the fact that in the benzene series the complete oxidation of methyl to carboxyl is an easily accomplished and common operation. The series of reactions may be illustrated, for the benzene compounds, as follows:



Oxidation of Hydrocarbons.—In this case also the first step does not take place, though the reverse, the reduction of **benzyl alcohol** to **toluene** is easily accomplished. The important fact now, in connection

with the aromatic acids, is, that a common general method of synthesizing them is by the oxidation of a methyl group to carboxyl and for each methyl group linked to a benzene ring a carboxyl group is the final oxidation product. In this way we may obtain not only mono- but also poly-carboxy acids. It is also true, that not only a single methyl group linked to a benzene ring, but any poly-carbon saturated side chain, will yield the carboxyl group as the final oxidation product. These relationships may be illustrated by reactions which have been previously referred to (p. 486), viz., that **toluene**, **methyl benzene**, yields **benzoic acid**, **carboxy benzene**; and **mesitylene**, **tri-methyl benzene**, yields successively a *mono-carboxy*, a *di-carboxy* and a *tri-carboxy* acid.



In our study of the aromatic aldehydes we have also stated that they are synthesized by the oxidation of benzene hydrocarbons containing an unsaturated side chain, in which the double bond is between the first and second carbons from the benzene ring. The aldehydes then being oxidizable to the acids gives us a second class of hydrocarbons from which the acids may be obtained by oxidation.



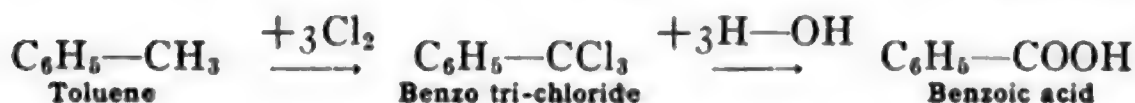
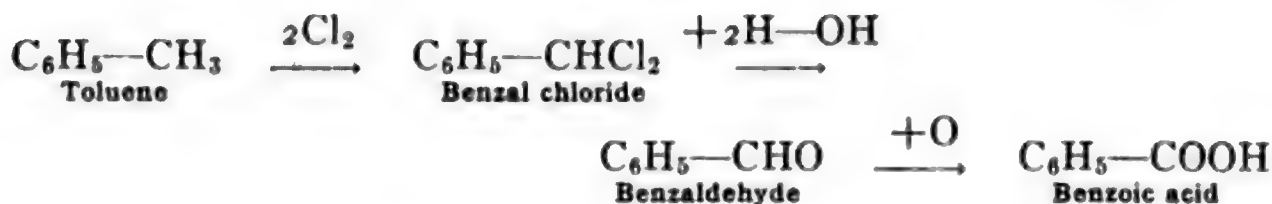
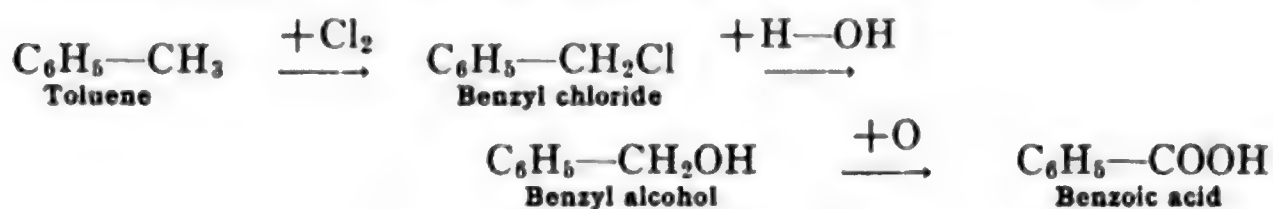
Thus we see that no matter what the nature of the side chain group in a benzene hydrocarbon, whether a single methyl group, a saturated poly-carbon chain or an unsaturated poly-carbon chain, each side chain always yields the *carboxyl* group as the final product. The intermediate products, however, and the ease with which the oxidation is effected varies with the character of the side chain so that in compounds containing two or more different hydrocarbon side chains one will be oxid-

ized more easily than another. In general we may say; (a) The longer side chain is always oxidized the more easily. (b) The side chain

containing a tertiary carbon group, $\left(-\text{CH} \begin{array}{l} \nearrow \text{C} \\ \searrow \text{C} \end{array}\right)$, is always more easily

oxidized than a single methyl group or a chain containing only primary or secondary carbon groups. (c) With saturated side chains the intermediate products are probably alcohols, the hydroxyl group being formed from a hydrogen of the carbon group linked to the ring, this alcohol group then oxidizing to the carboxyl group. (d) With unsaturated side chains the intermediate product is an aldehyde which then oxidizes to the acid.

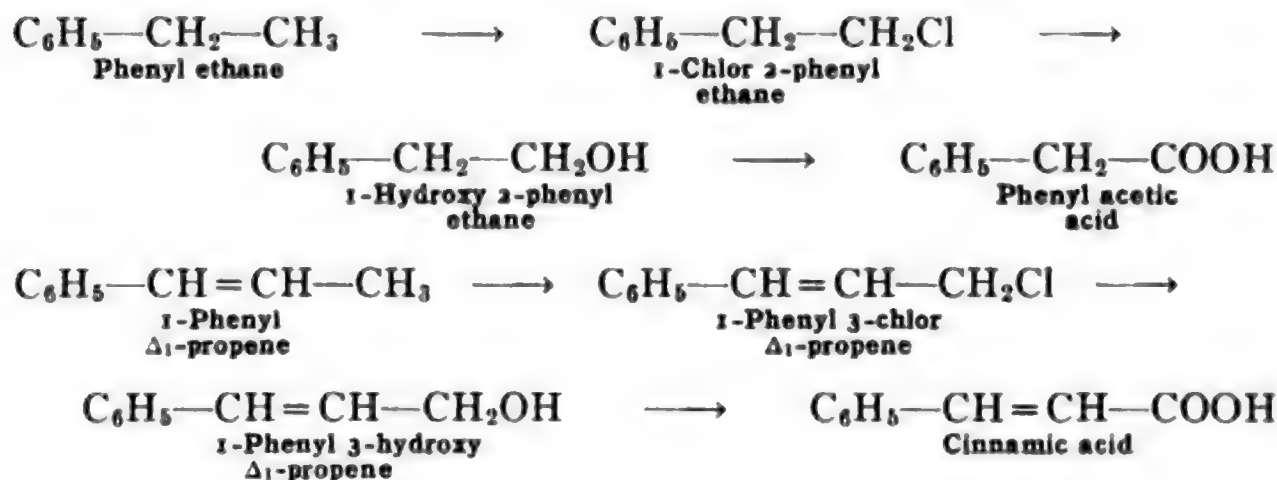
Halogen Substitution and Oxidation.—In the oxidation of these hydrocarbons to the corresponding acids the reaction may be accomplished with a variety of reagents. Toluene, for example may be oxidized to benzoic acid by means of dilute nitric acid or chromic acid. In the case of ring substituted hydrocarbons the oxidation is even more easily effected and potassium permanganate may be used. The oxidation is often accomplished more easily by indirect processes. Chlorine may be first substituted in the side chain and then the chlorine product by hydrolysis yields either an alcohol or an aldehyde. These are then oxidized, often by means of the chlorine first used as a substituting agent, yielding finally the acid. In the case of **benzo tri-chloride** the chlorine substitution product yields the acid directly by hydrolysis.



Ring Carboxyl.—In all of the cases cited the acid resulting is a ring carboxy benzene product and such an acid will always result from

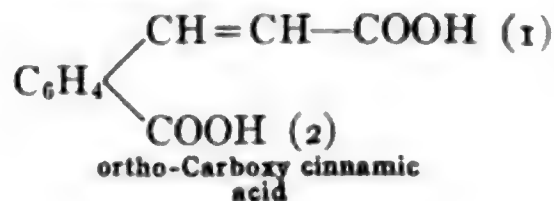
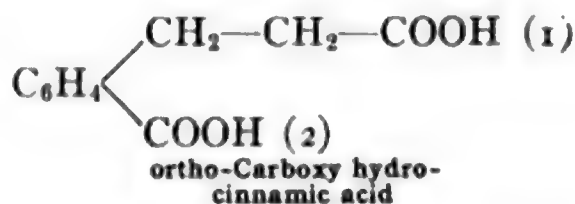
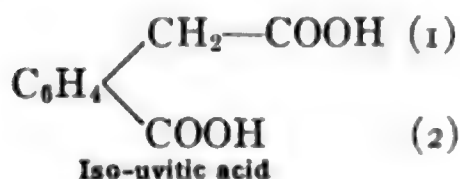
the oxidation of any side chain or from the chlorination and subsequent oxidation of a single carbon side chain, *i.e.*, *methyl*.

Side-chain Carboxyl.—If, however, the side chain consists of more than one carbon group the halogenation and subsequent oxidation will result in another type of aromatic acid if the halogen is at the end of the chain and possible of yielding a primary alcohol or an aldehyde.



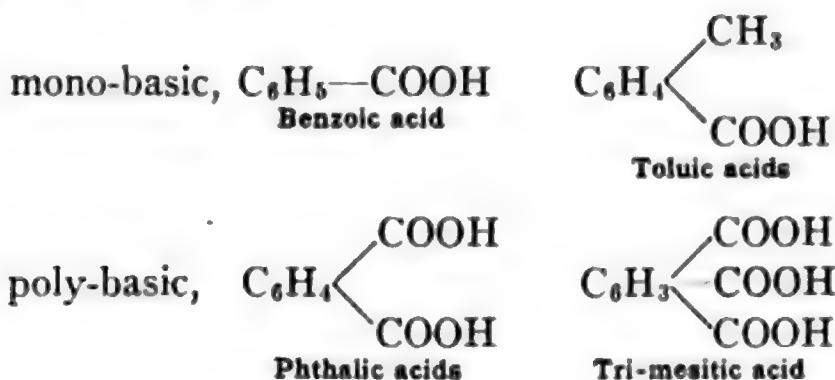
In such a product the carboxyl group instead of being in the ring is in the side chain and while it is considered as an aromatic acid it is really a benzene derivative of an aliphatic acid and has the character and properties of such an acid, its synthesis as above being exactly analogous to the general method of synthesizing aliphatic acids. Such acids also may be either *mono-carboxy* or *poly-carboxy* if the character of the side chain is branched, giving more than one end carbon group and making more than one carboxyl group possible.

Mixed Ring and Side-chain Carboxyl.—Still a third type of aromatic acid is possible, *viz.*, one in which both of the preceding types are present, *i.e.*, one or more carboxyl groups may be in the ring and at the same time one or more may be in the side chain, *e.g.*,

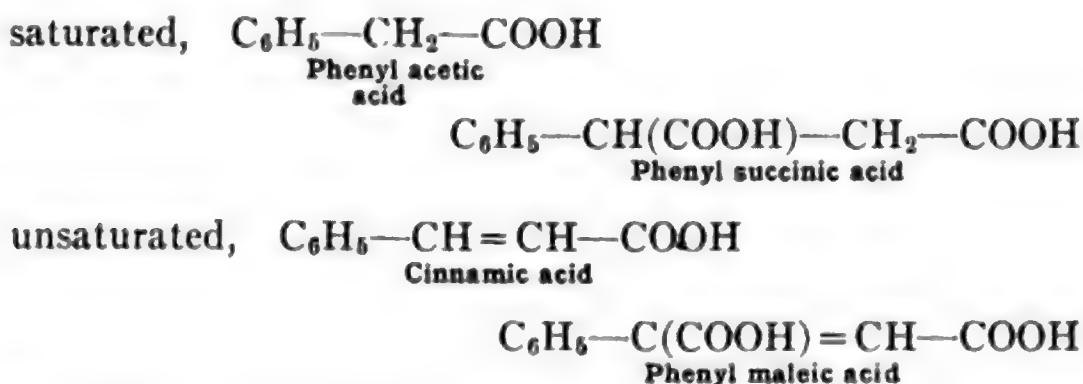


We can readily see what a variety of acids are possible in the benzene series. Not all of the types mentioned have individual members of sufficient importance to be taken up in detail, but the foregoing discussion will illustrate the scope of the group. For the sake of clearness we may summarize the classes of aromatic acids with the following examples.

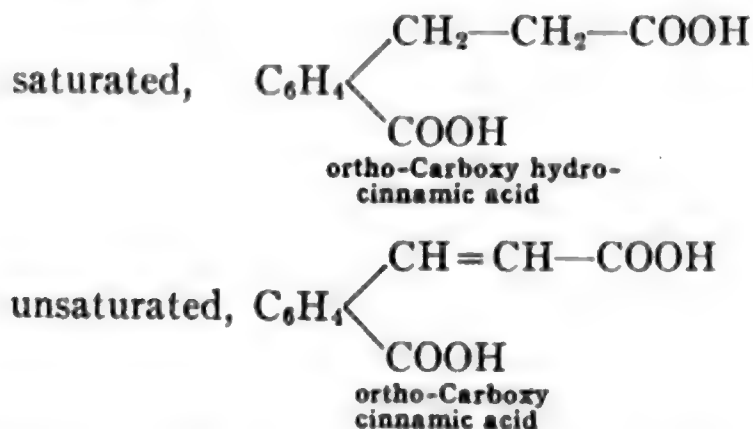
I. Ring Carboxy Acids.



II. Side-chain Carboxy Acids.



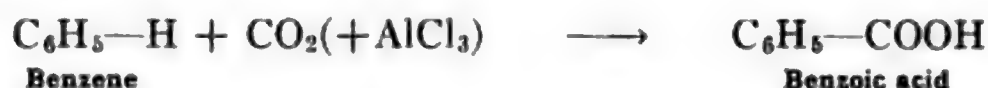
III. Mixed Ring and Side-chain Carboxy Acids.



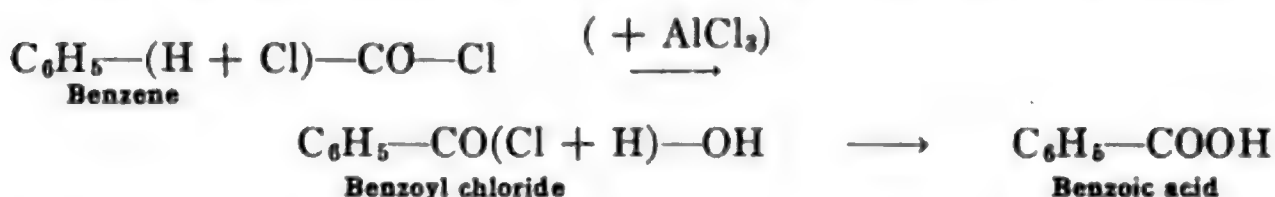
Synthesis of Ring Carboxy Acids.—We have just discussed the synthesis of aromatic acids by the oxidation of benzene hydrocarbons containing a side chain. As would be expected from our description

of the different types of these acids the methods of synthesis are several. The two distinct types, viz., those in which the carboxyl group is in the ring and those in which the carboxyl group is in the side chain, will naturally be formed by different kinds of reactions; the former by those characteristic in general of benzene compounds, the latter by those characteristic of aliphatic compounds and which are used in synthesizing aliphatic acids.

From Hydrocarbons, Friedel-Craft.—The aromatic *hydrocarbons* yield ring carboxy acids by other reactions than those effecting oxidation of a side chain. **Carbon dioxide** may be introduced directly into a benzene ring, thus converting a hydrogen into carboxyl. This may be accomplished in the presence of aluminium chloride, **Friedel-Craft reagent**.

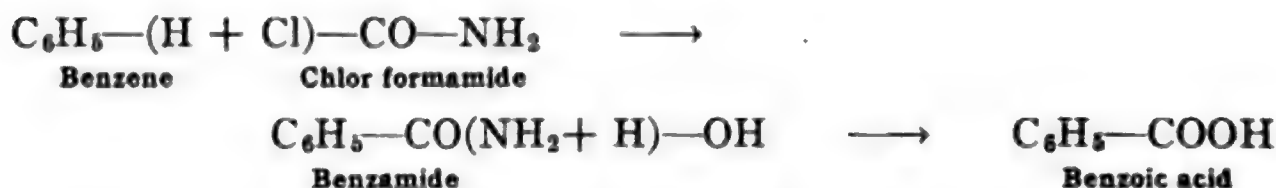


The intermediate products are complex compounds containing aluminium, but the end product is the acid as above. The same result is accomplished if **carbonyl chloride**, COCl_2 , is used instead of carbon dioxide, the first formed acid chloride being hydrolyzed to the acid.



This reaction does not yield good results because the acid chloride reacts with the hydrocarbon forming a ketone.

Gattermann Synthesis.—Still another reaction accomplishes the same purpose. This is by the use of **chlor formamide**, Cl—CO—NH_2 , and is similar to the reaction with carbonyl chloride. It yields first the *acid amide* which is hydrolyzed to the acid.



This is known as the **Gattermann synthesis** and yields better results than the preceding synthesis.

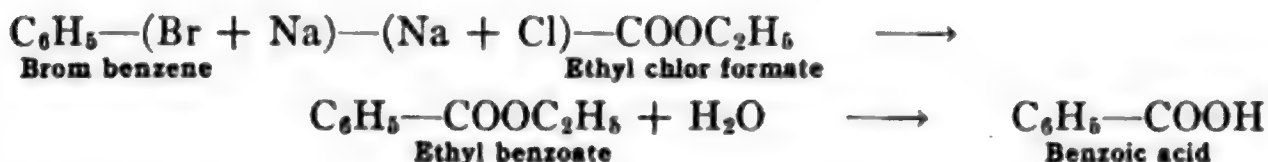
From Aryl Halides. Kekulé Synthesis.—*Aromatic halides* in which the halogen is in the ring yield ring carboxy acids by the action of carbon dioxide and sodium.



The reaction is known as the **Kekulé synthesis** and is analogous to the formation of aliphatic acids by the action of carbon dioxide on *sodium alkyls* (p. 132).

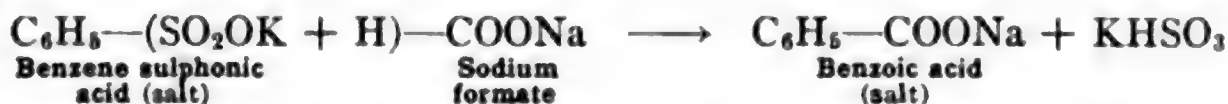


Wurtz Synthesis.—The introduction of carboxyl in place of a halogen in the ring may also be effected by the action of an ester of chlor formic acid and sodium.



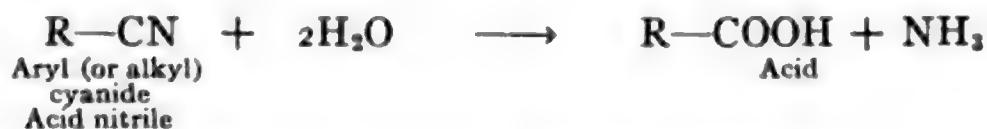
This synthesis was first carried out by **Wurtz** and is known by his name. It is similar to the like synthesis of hydrocarbons (p. 16).

From Sulphonic Acids.—When a salt of a *sulphonic acid* is fused with sodium formate the sulphonic acid group is replaced by the carboxyl group.



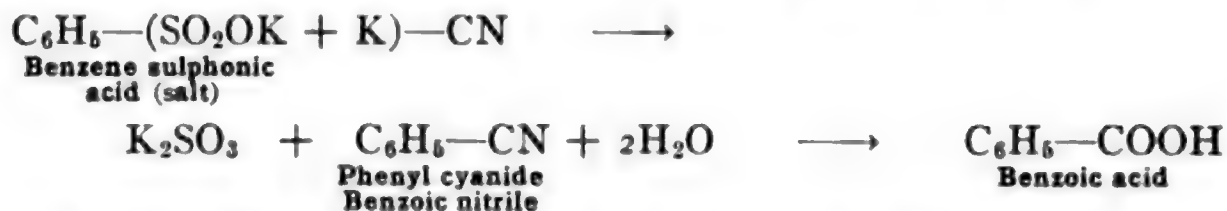
This is similar to the use of chlor formic acid and chlor formamide in the preceding syntheses. The method was first used by **Victor Meyer**. Sulphonic acids are also the starting point for the synthesis of acids through the intermediate acid nitrile as described next.

From Aryl Cyanides (Acid Nitriles).—The aromatic cyanides which were simply referred to as substitution products (p. 521) are, of course, like the aliphatic cyanides, nitriles of acids which they yield on hydrolysis.



They are thus a general source for the synthesis of acids.

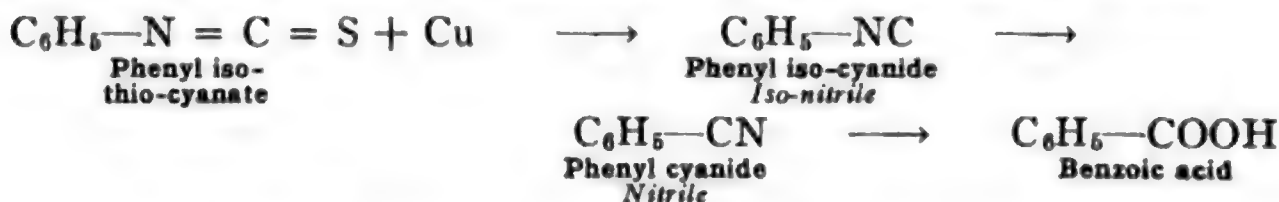
Nitriles from Sulphonic Acids or Aryl Halides.—Individual acid nitriles will be mentioned at various times whenever they are used in preparing various acids. Several reactions may be employed to prepare the nitriles in which the cyanogen group is in the ring. The simplest method is from sulphonic acids by heating with potassium cyanide.



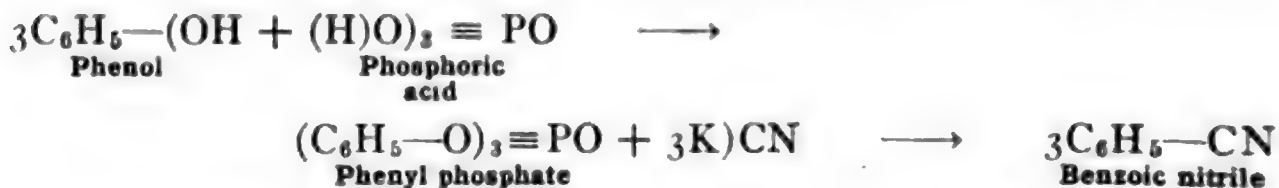
The synthesis of the acid from the nitrile thus becomes in reality a synthesis from sulphonic acids. An exactly analogous reaction takes place when an aryl halide, with the halogen in the side chain, is distilled with potassium cyanide, as discussed later (p. 678).



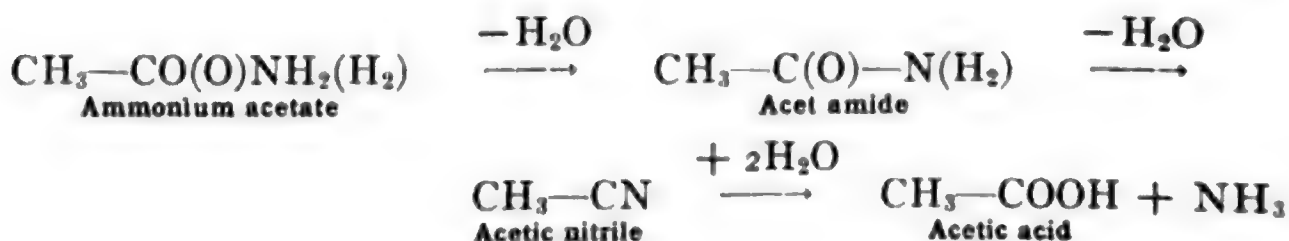
Nitriles from Iso-thio-cyanates.—The nitriles may also be made from iso-thio-cyanates (p. 73). When these are heated with copper the sulphur is eliminated and the *iso*-cyanides or *iso*-nitriles are obtained and these iso-cyanides are transformed into the *cyanide* or *nitrile*.



From Phenol Esters.—Another method of preparing nitriles is by the action of potassium cyanide on the phosphoric acid esters of phenols.

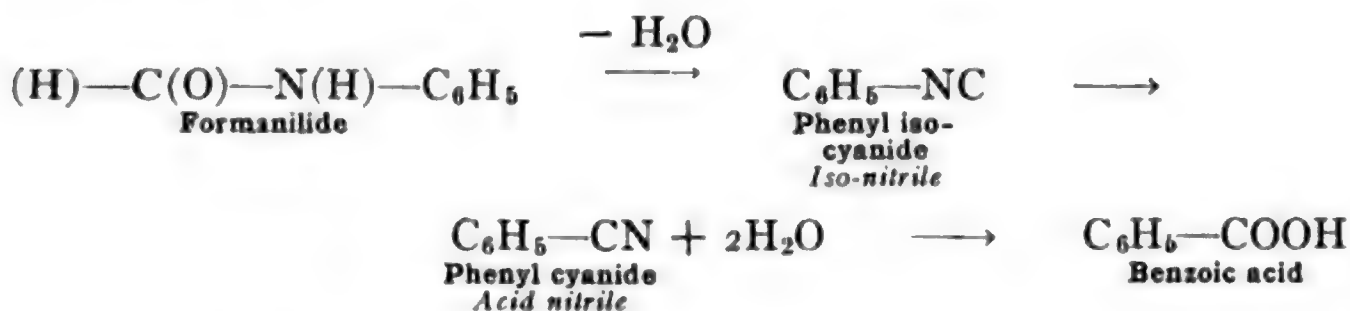


From Acid Amides and Anilides.—In the aliphatic series the *cyanides* are formed from the *acid amides* by loss of water, the amides themselves resulting from the ammonium salts by a similar loss of water.

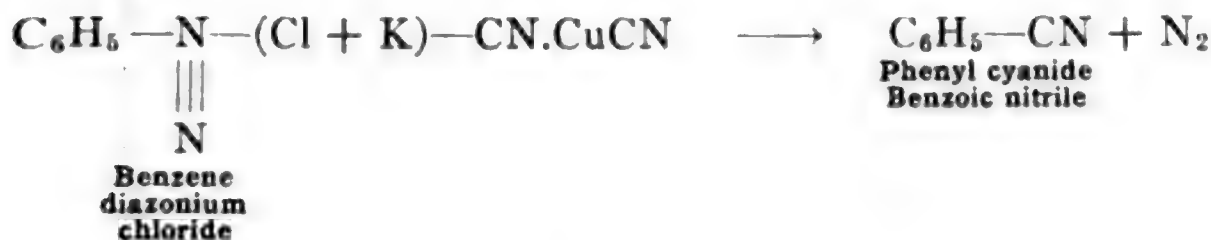


This shows the relationship of these compounds to each other as was fully discussed in Part I (p. 148).

In the aromatic series the direct conversion of acid amides into acid nitriles does not take place readily; but the acid itself is made from the acid amide by the reverse process as indicated above, viz., by hydration to the ammonium salt of the acid, which then yields the acid. A related method, however, is used for preparing acids from *anilides* of **formic acid**. Aniline being an ammonia compound yields acid-amide-like products with aliphatic acids, *e.g.*, acet anilide, $\text{CH}_3\text{—CO—NH—C}_6\text{H}_5$ (p. 556). Such a compound can not, however, lose water in the same way as the acid amide in the above reaction for the ammonia residue in an anilide contains only one hydrogen. Nevertheless anilides lose water but in a different way. In the case of the anilide of formic acid, *i.e.*, **formanilide**, $\text{H—CO—NH—C}_6\text{H}_5$, the loss of water results in a compound in which the carbon and nitrogen remain linked to the benzene ring and an *iso-cyanide* or *iso-nitrile* is formed. The *iso-nitrile* is readily converted into the nitrile and the acid may then be obtained from that.

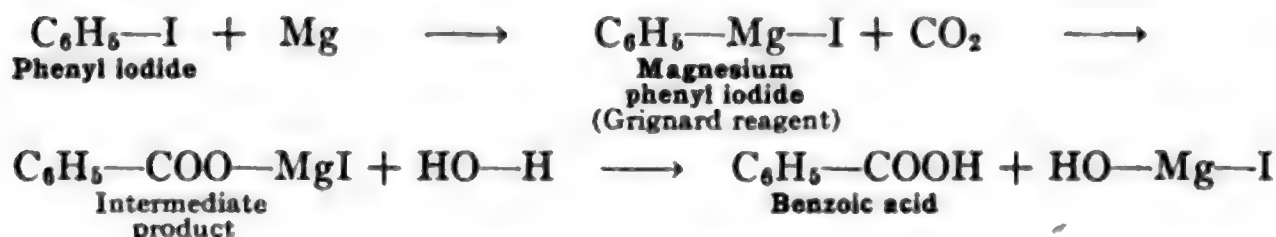


From Diazo Compounds.—The diazo compounds may also be used as intermediate products to obtain the acid nitriles and thus the acids. The reaction already discussed under diazo compounds (p. 599) is the **Gattermann reaction** with **cuprous potassium cyanide**, KCN.CuCN , by which the *diazo group* is replaced by the *cyanogen group*.



Ring Carboxy Acids by the Grignard Reaction.—Aromatic acids with carboxyl in the ring may also be prepared by the **Grignard reaction**

by the direct introduction of carbon dioxide into an *aryl magnesium halide*, Grignard reagent.

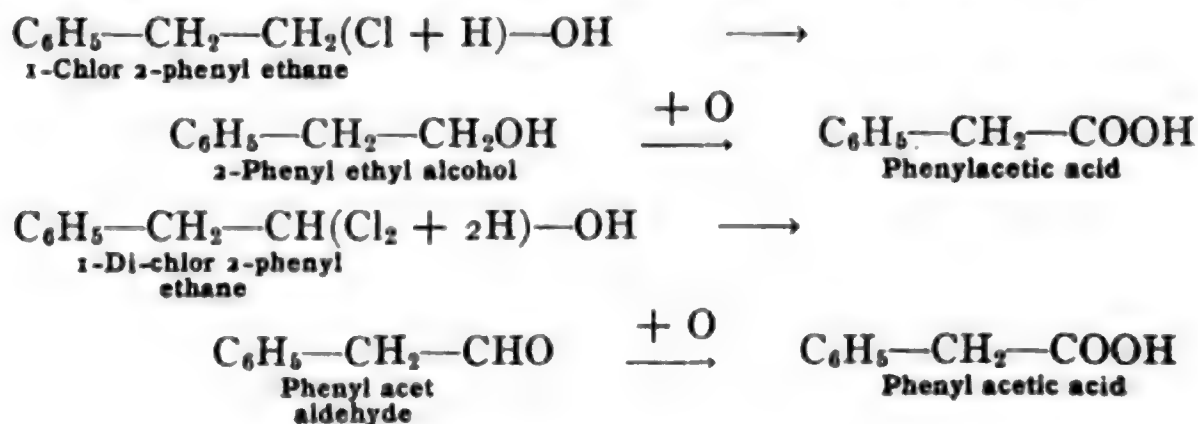


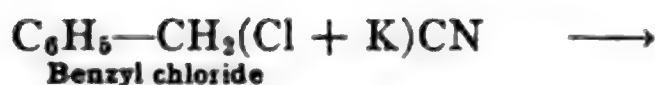
A secondary reaction between the intermediate product and the Grignard reagent causes other products, alcohols and ketones, to be formed at the same time especially with the bromide reagent.

Synthesis of Side-chain Carboxy Acids.—The *side-chain carboxy acids* being really *aryl substituted* aliphatic acids are synthesized by methods characteristic of such acids.

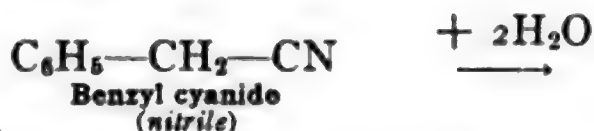
From Aryl Halides.—The most important method has already been discussed, viz., from halogen substituted benzene hydrocarbons in which the halogen is in the side chain. This side chain must have more than one carbon group otherwise the product will be a ring carboxy acid. The halogen compound with water yields the hydroxyl compound or alcohol and if the halogen and therefore the hydroxyl is in an end carbon group the resulting alcohol will be primary, yielding an aldehyde and then acid on not too strong oxidation. If the oxidation is complete the entire chain becomes oxidized to carboxyl and a ring carboxy acid results. If the halogen is not in an end carbon group of the side chain it may still yield an acid, not by conversion into the alcohol, aldehyde and then acid; but by replacing the halogen with cyanogen yielding an acid nitrile, which then, on hydrolysis, gives an acid.

In this case the carbon groups in the side chain become increased in number by one so that this method may be used in case the side chain has only one carbon. These syntheses may be illustrated as follows:

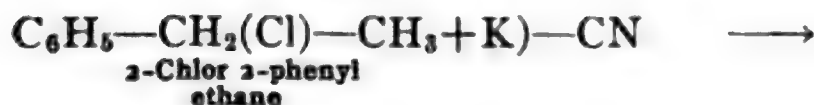
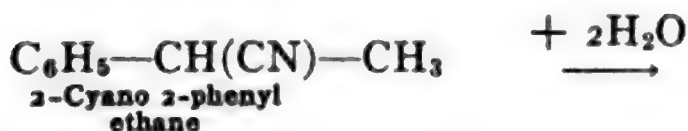
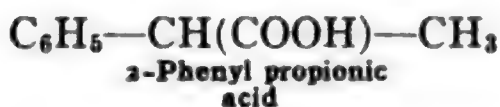




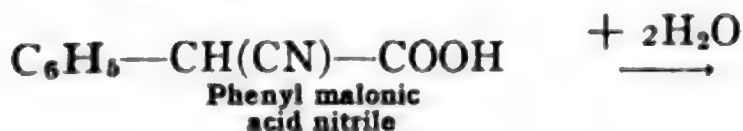
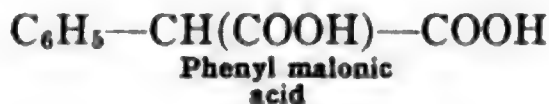
Benzyl chloride

Benzyl cyanide
(nitrile)

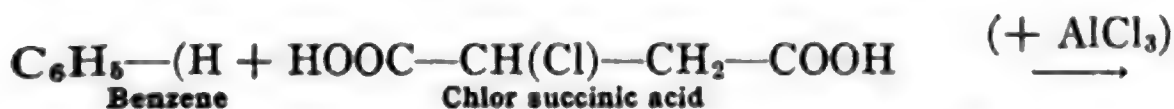
Phenyl acetic acid

2-Chlor 2-phenyl
ethane2-Cyano 2-phenyl
ethane2-Phenyl propionic
acid

Phenyl chlor acetic acid

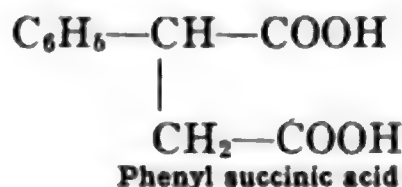
Phenyl malonic
acid nitrilePhenyl malonic
acid

From Aliphatic Acids.—By the introduction of an aryl radical into an aliphatic acid we may obtain side-chain carboxy acids in which the side chain is the same as in the aliphatic acid. This reaction is effected by the **Friedel-Craft** reagent, aluminium chloride, with the aromatic hydrocarbon together with a halogen aliphatic acid.



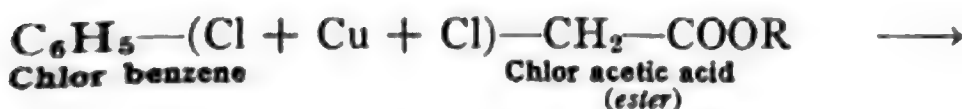
Benzene

Chlor succinic acid

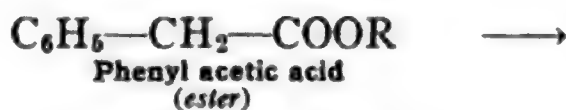


Phenyl succinic acid

The same result may be accomplished by using an aryl halide and copper with the halogen aliphatic ester.

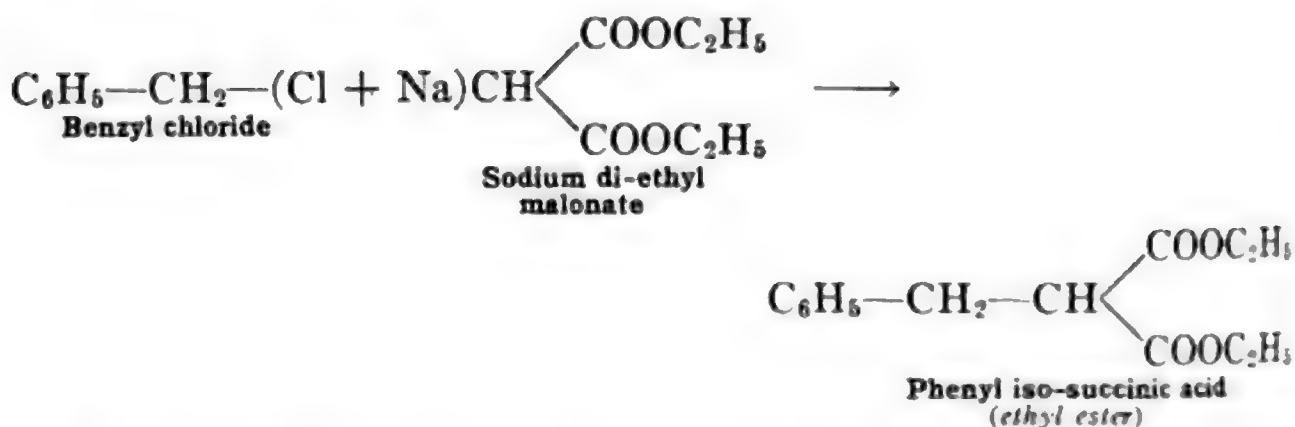


Chlor benzene

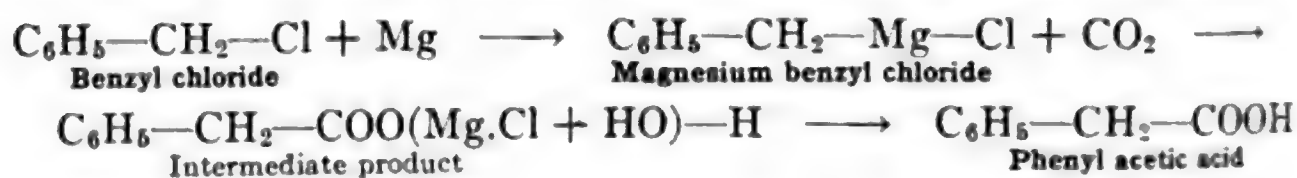
Chlor acetic acid
(ester)Phenyl acetic acid
(ester)

Phenyl acetic acid

With Malonic Ester.—The *malonic ester synthesis* (p. 274) is also applicable in this case, the sodium malonic ester reacting with aryl halides just as it does with alkyl halides.



By Grignard Reaction.—Exactly analogous to the **Grignard** synthesis of ring carboxy acids is the synthesis of side-chain carboxy acids by the introduction of carbon dioxide into the **Grignard** reagent.



After the preceding general discussion of aromatic acids only a few of the many that are known need to be discussed in detail with a consideration of their derivatives. Those to be studied are:

Ring carboxy acids

Mono-basic,	Benzoic acid,	$\text{C}_6\text{H}_5\text{—COOH}$
Di-basic,	Phthalic acids,	$\text{C}_6\text{H}_4 \begin{array}{l} \text{COOH} \\ \text{COOH(o)(m)(p)} \end{array}$

Side-chain carboxy acids

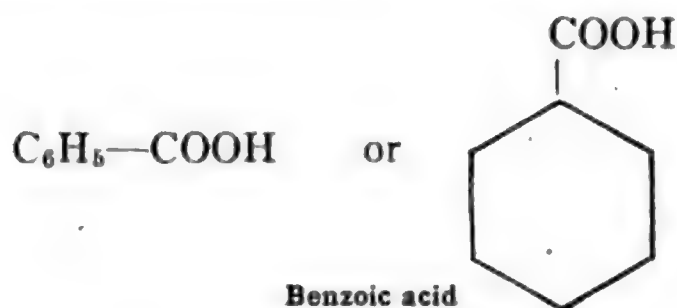
Saturated,	Phenyl acetic acid,	$\text{C}_6\text{H}_5\text{—CH}_2\text{—COOH}$
	Hydro cinnamic acid,	$\text{C}_6\text{H}_5\text{—CH}_2\text{—CH}_2\text{—COOH}$
Unsaturated,	Cinnamic acid or	$\text{C}_6\text{H}_5\text{—CH=CH—COOH}$
	Phenyl acrylic acid	
	Phenyl propiolic acid,	$\text{C}_6\text{H}_5\text{—C}\equiv\text{C—COOH}$
	Phenyl vinyl acetic acid,	$\text{C}_6\text{H}_5\text{—CH=CH—CH}_2\text{—COOH}$

Benzoic Acid, $\text{C}_6\text{H}_5\text{—COOH}$, and Derivatives

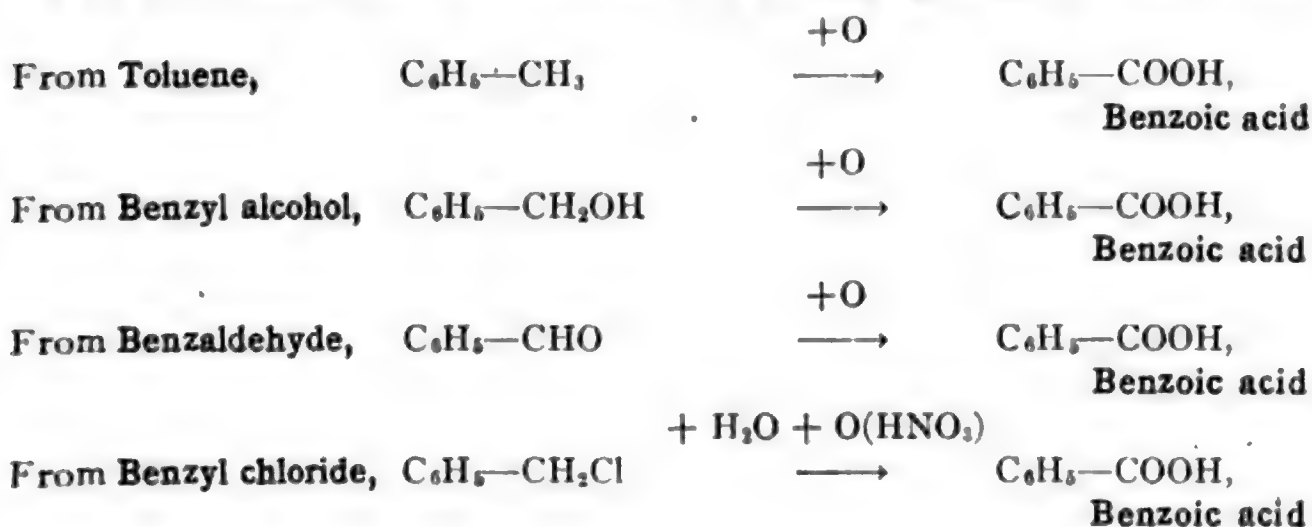
Occurrence.—**Benzoic acid** is a naturally occurring substance being found both free and as esters in *gum benzoin*, *Peru* and *Tolu balsam*, *huckleberries*, the flower, *dragon's blood*, etc. It also occurs in combina-

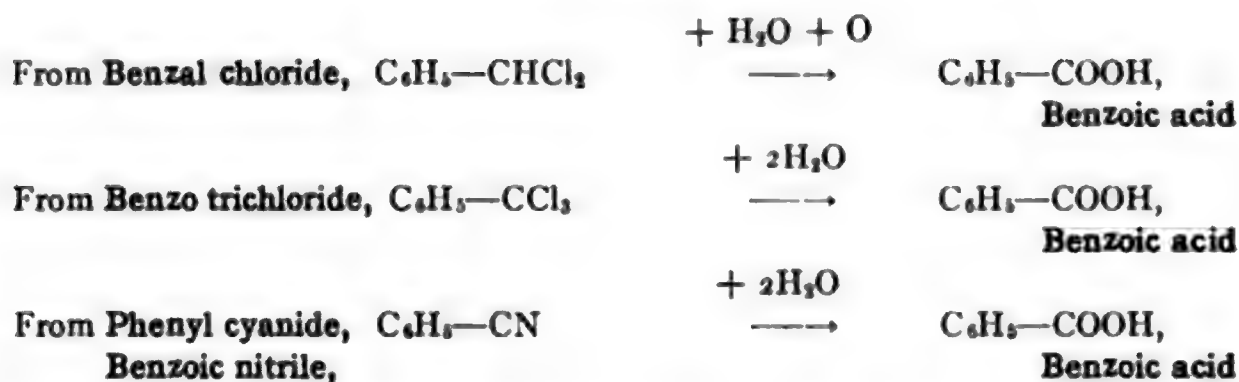
tion as **hippuric acid** which is present in large amounts in the urine of herbivorous animals and in very small amounts in human urine. Benzoic acid is of especial interest historically associated with benzaldehyde (p. 655) because of **Liebig** and **Wöhler's** classic investigation on "**The Radical of Benzoic Acid**" which did so much toward establishing the theory of radicals (p. 14). It is a solid, crystalline substance forming glistening crystals, m.p. 121° , b.p. 249° . It sublimes below its melting point at 100° and is also volatile with steam, the vapor being irritating. It is soluble in 375 parts of water at ordinary temperatures and in 45 parts at 75° . In alcohol and ether it is quite easily soluble. The natural sources from which it is usually obtained are gum benzoin and hippuric acid. From the former, in which it is present in the free condition, it is obtained by heat, the acid subliming; or the gum is heated with lime in which case the acid is obtained as the calcium salt on extraction of the heated mass. To get the acid from hippuric acid the latter, which is an acid amide derivative, is hydrolyzed with dilute acids, the benzoic acid being thus set free.

Syntheses.—The important synthetic methods for its preparation have all been discussed and from them and the reactions and derivatives of the acid its constitution has been fully established as **mono-carboxy benzene**.



The syntheses may be reviewed by simply giving the reactions.

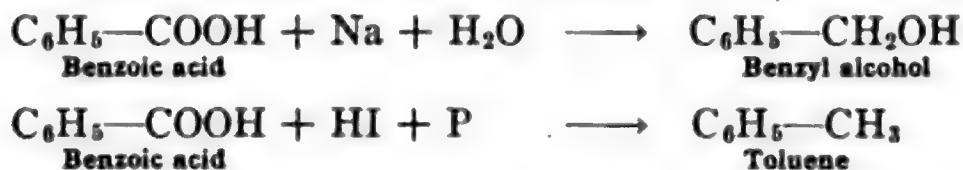




The most common synthesis commercially is the first one from toluene either by direct oxidation or through one of the intermediate chlorides.

In its chemical properties benzoic acid reacts exactly as the aliphatic mono-carboxy acids yielding the following derivatives: salts, esters, acid anhydride, acid chloride, acid amide, acid anilide, benzoyl derivatives, etc.

Reduction.—On reduction with sodium the acid yields the corresponding alcohol, **benzyl alcohol**, which by **hydrogen iodide** and **phosphorus** is further reduced to the hydrocarbon **toluene**. This last reducing agent also reduces the acid directly to the hydrocarbon.



Salts.—Most of the salts of benzoic acid are easily soluble compounds. Sodium benzoate is used as a preservative.

Benzene from Benzoic Acid.—Just as salts of **acetic acid** yield **methane** by the loss of carbon dioxide when heated with lime so benzoic acid salts yield **benzene**.



Benzophenone from Benzoic Acid.—Also as **calcium acetate** on heating yields **acetone** so calcium benzoate yields **diphenyl ketone** or **benzophenone**.



Esters.—The *esters* of benzoic acid are not of special importance. The *methyl*, *ethyl*, *phenyl* and *benzyl* esters are found in certain plants

and plant resins. They all have pleasant odors and are formed in making qualitative and quantitative determinations of the acid.

Benzoyl Chloride.—The *acid chloride* of benzoic acid, **benzoyl chloride**, $C_6H_5-CO-Cl$, is readily formed by the action of **phosphorus pentachloride** on the acid.



It is an oily liquid with a strong irritating odor, m.p. -1° , b.p. 198° . With alcoholic hydroxyl compounds benzoyl chloride acts exactly as acetyl chloride does and the *benzoyl group*, C_6H_5-CO , is introduced in place of the hydroxyl hydrogen forming *esters*.



Benzoylation.—The introduction of the *benzoyl* radical for alcoholic hydrogen is termed *benzoylation* corresponding to *acetylation* or the introduction of the *acetyl* radical in the aliphatic compounds. The action of benzoyl chloride is more moderate than that of acetyl chloride and furthermore the products are often crystalline and, therefore, readily identified. These facts often make it more desirable to *benzoylate* an hydroxyl or amino compound than to *acetylate* it, when it is necessary to know whether an unknown substance is an alcoholic hydroxyl compound or an amino compound, and how many of such groups are present (p. 318).

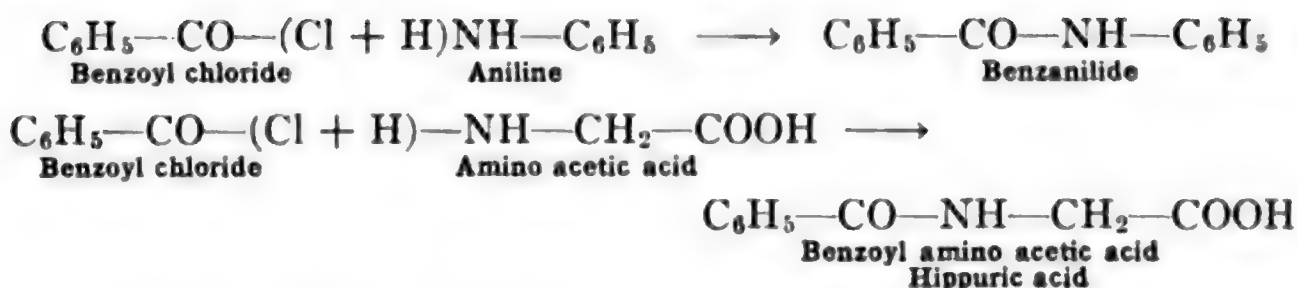
Benzoic Anhydride.—The anhydride of benzoic acid is exactly analogous to acetic anhydride and is formed by the same kind of reaction.



In the aliphatic series acetylation is better effected by means of **acetic anhydride** than of acetyl chloride. With the benzene compounds, however, the acid chloride is better than the anhydride.

Benzoyl Amino Compounds.—Benzoyl chloride also reacts with **ammonia**, **aniline** and **amino acids** yielding acid amide compounds.





Schotten-Baumann Reaction.—In practice these reactions take place in the presence of sodium hydroxide, the reaction being known as the **Schotten-Baumann** reaction.

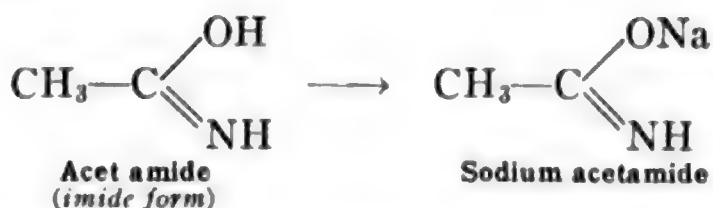
Benzamide.—The amide of benzoic acid is formed by the reaction given above and also by the action of **chlor formamide** on **benzene**.



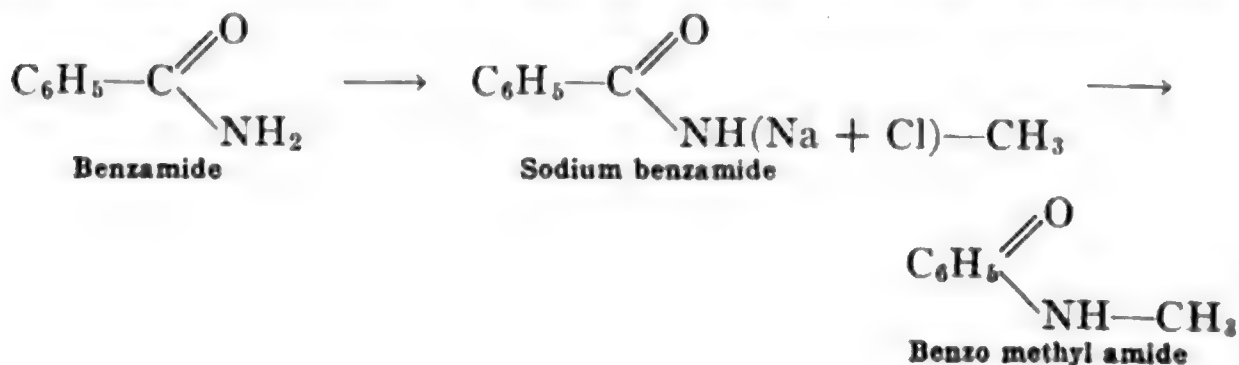
This, it will be recalled, is the first step in the **Gattermann synthesis** of benzoic acid (p. 674). Another method for preparing benzamide is by the taking up of water by benzoic nitrile which is in agreement with the relation of these compounds. The reaction occurs when the nitrile is treated with an alkaline solution of hydrogen peroxide.



Metal Salts.—In discussing the constitution of **acet amide** (p. 146) the formation of metal salts raised the question as to the true constitution of the amide, the tautomeric hydroxy imide formula being probable in this reaction.

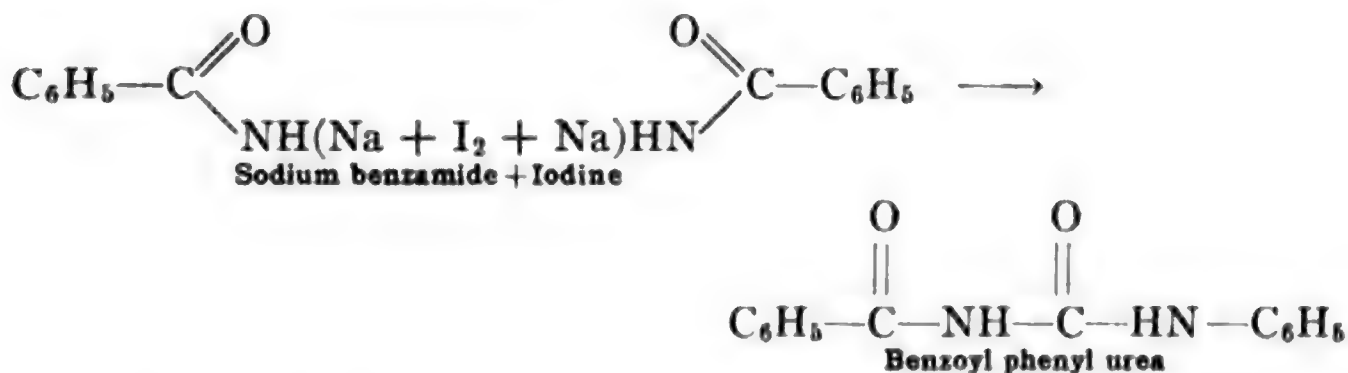


Now **benzamide** forms similar metallic salts and these salts when treated with *alkyl halides* yield *alkyl amine* derivatives of benzoic acid.

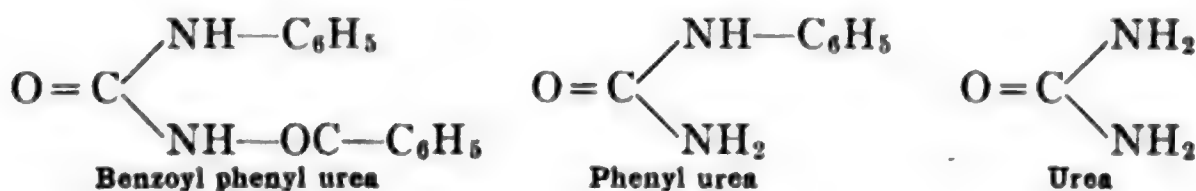


This reaction proves that in the **sodium benzamide** the sodium is linked to nitrogen not to oxygen.

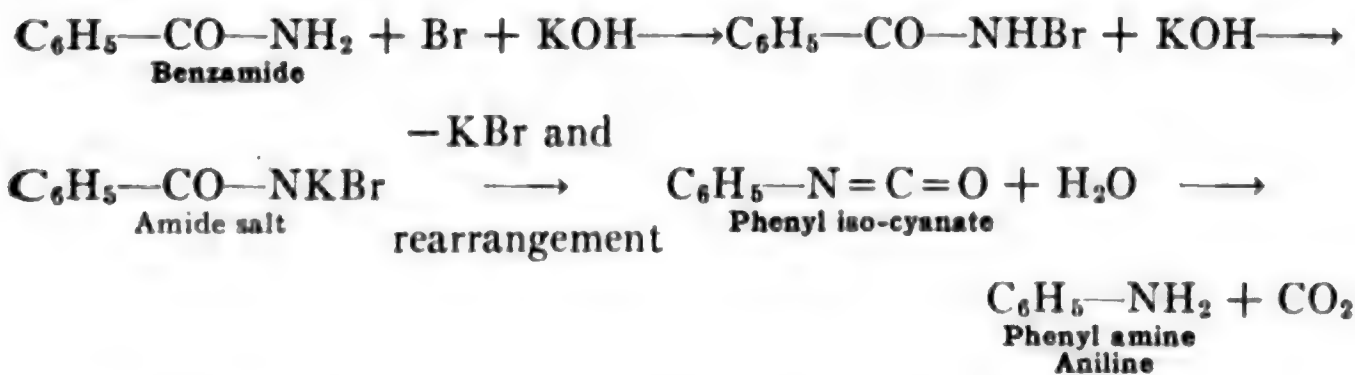
Benzoyl Phenyl Urea.—When this sodium salt of benzamide is treated with **iodine** two sodium atoms are lost from two molecules, a rearrangement occurs and the two molecules unite.



If the formula is written differently it will be seen better as a urea derivative.

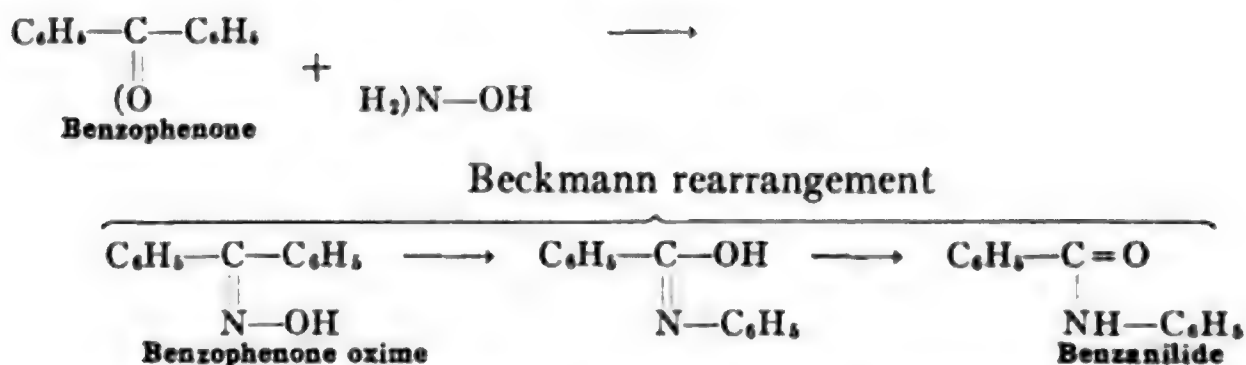


Hofmann Reaction.—The metallic salts of benzamide are also involved in the **Hofmann reaction** (p. 148), by which an acid amide is converted into a primary amine.

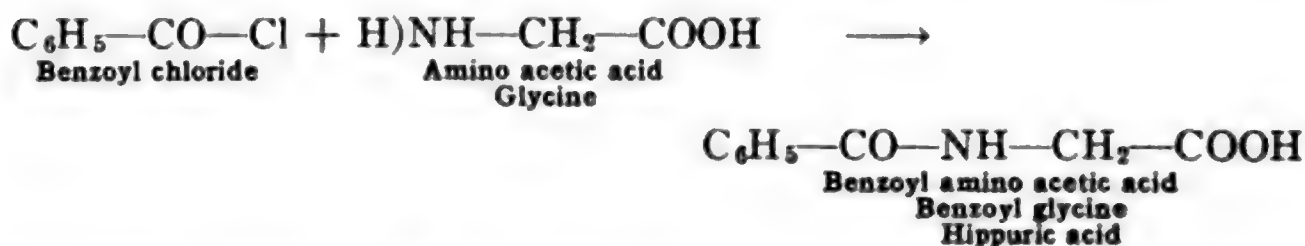


Benzanilide.—Analogous to benzamide is the aniline derivative of benzoic acid, viz., benzanilide, $\text{C}_6\text{H}_5-\text{CO}-\text{NH}-\text{C}_6\text{H}_5$, which is formed by the reaction previously given (p. 684) from benzoyl chloride and aniline.

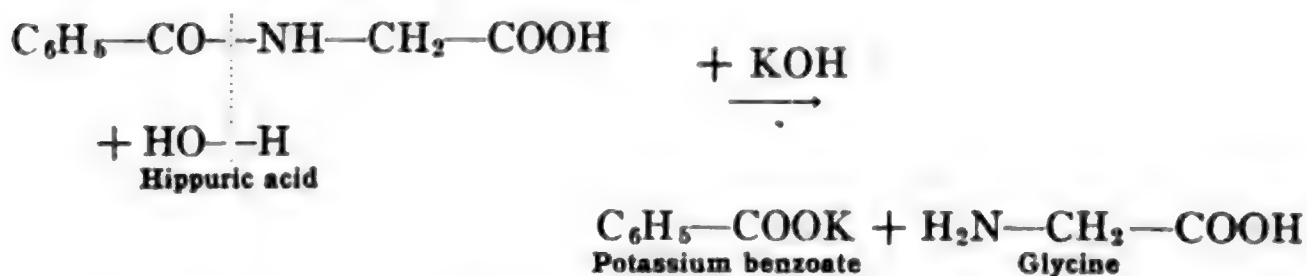
Beckmann Rearrangement.—The special interest in connection with this compound is its formation from **benzophenone oxime** by the **Beckmann rearrangement** (p. 654).



Hippuric Acid.—When the benzoyl group is introduced into an amino acid in place of an amino hydrogen, by means of the **Schotten-Baumann reaction**, a **benzoyl amino acid** is obtained. With **amino acetic acid** or **glycine** (p. 388) the product is **benzoyl amino acetic acid** or **benzoyl glycine**, also known as **hippuric acid**.



When hydrolyzed with dilute potassium hydroxide the products are **potassium benzoate** and **glycine**.



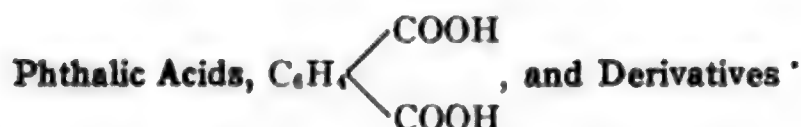
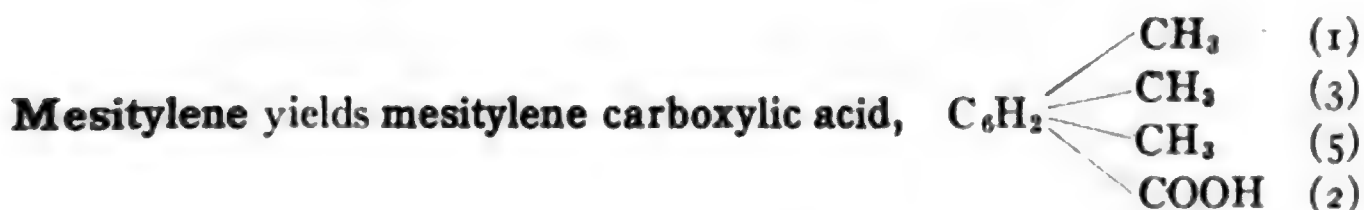
Thus both by its synthesis and by its hydrolytic products hippuric acid is proven to be **benzoyl glycine**.

As early as 1776 hippuric acid was found in the urine of cows, and in 1829 **Liebig** showed that it was a benzoic acid derivative. In 1846 **Dessaigues** established its constitution as **benzoyl glycine**. As a natural physiological excretion product it is a source of both benzoic acid and of glycine. In human urine it is present to the amount of about 0.7 gram per day, *i.e.*, about 0.05 to 0.07 per cent. The amount excreted per day may be noticeably increased by eating **benzoic acid** or other compounds which can yield a benzoyl group, *e.g.*, **cinnamic acid** or **toluene**. As benzoic acid or some other benzene compound is usually present in plant food materials and as glycine is a product of

protein hydrolysis the hippuric acid in the animal body is undoubtedly synthesized from these two sources and is, therefore, naturally more abundant in the urine of herbivorous animals. An interesting fact in connection with the physiological synthesis of hippuric acid is the fact that birds which, like man, normally excrete practically no hippuric acid, when fed benzoic acid still excrete no hippuric acid. Instead a related **di-benzoyl** derivative of **di-amino valeric acid** known as **ornithuric acid** is obtained. From this it would appear that glycine is not a protein cleavage product in birds as in herbivorous animals and in man.

Toluic Acids, Xyloic Acids, Mesitylene Carboxylic Acid

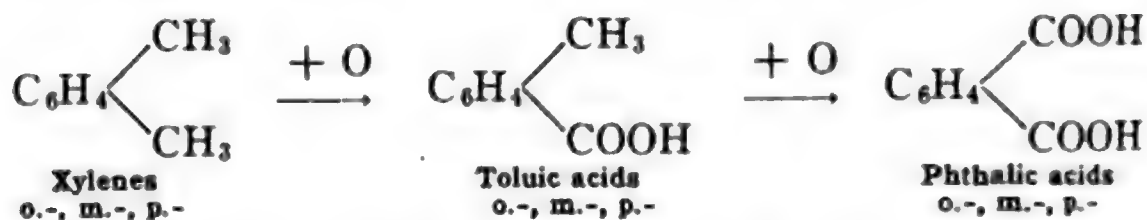
Mono-basic ring carboxy acids of the benzene homologues need only to be mentioned.



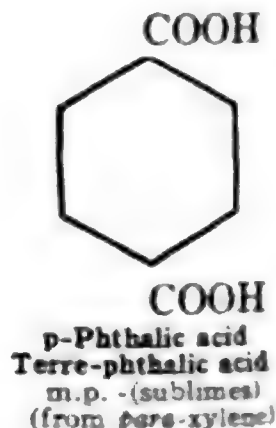
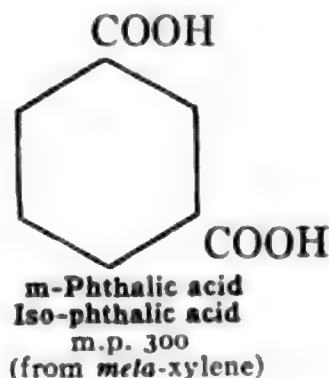
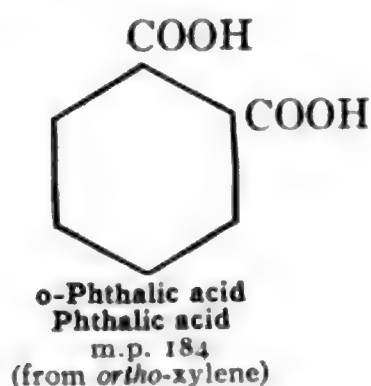
The only other ring carboxy acids to be considered in detail are the three **phthalic acids**. They all have the constitution of **di-carboxy benzene**, $\text{C}_6\text{H}_4 = (\text{COOH})_2$, and therefore three isomers are possible, *ortho*, *meta* and *para*.

Relation to Xylene.—Just as **toluene**, **mono-methyl benzene**, on oxidation of the methyl group to carboxyl yields **benzoic acid**, **mono-carboxy benzene**, so the three isomeric **xylenes**, **di-methyl benzenes**,

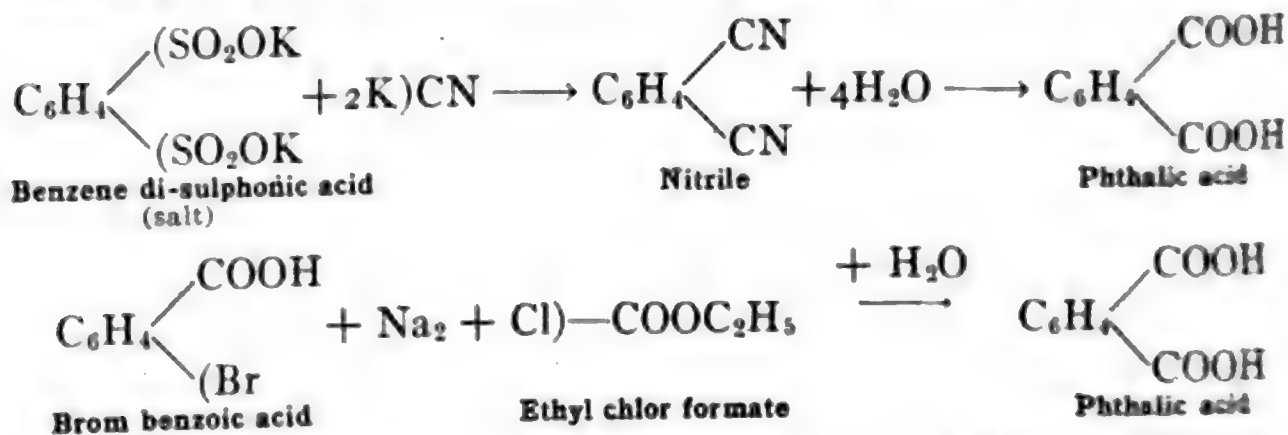
yield by similar oxidation three **di-carboxy benzenes**, with the three **mono-carboxy, or toluic, acids** as intermediate products.



This relation of the three phthalic acids to the three xylenes has been fully established and the exact constitution of each set of isomers is positively proven. This has been dwelt upon in our general discussion of the isomerism of di-substitution products of benzene and of the methods of orientation by which the position of the substitution groups is determined (p. 482). The full constitution and names of the three phthalic acids are:

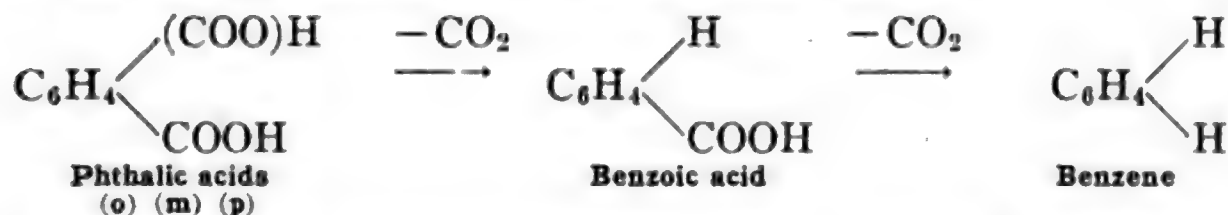


The general methods for synthesizing ring carboxy acids are applicable to the phthalic acids if we start with the corresponding di-substituted benzenes or with the mono-substituted benzoic acids, *e.g.*,



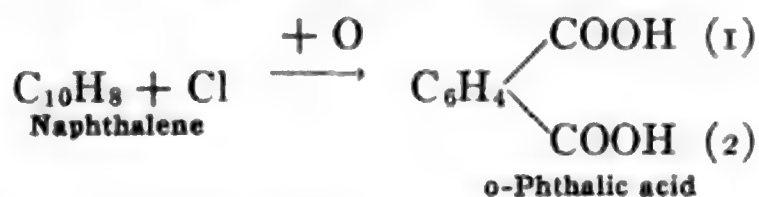
Like di-basic acids in general the phthalic acids yield both mono- and di-derivatives, *e.g.*, salts, esters, acid chlorides, acid amides. When heated with lime the acids lose two molecules of carbon dioxide and yield benzene just as benzoic acid does by the loss of one molecule.

The two molecules of carbon dioxide may be lost successively and benzoic acid will be obtained as an intermediate product.



It is plain that the three isomeric phthalic acids all yield the same benzoic acid, there being only one, the possibility of isomerism disappearing as soon as one carboxyl group is converted into hydrogen. If, however, the phthalic acids are reduced and the carboxyl groups converted successively or together into aldehyde or primary alcohol groups and finally to methyl groups, yielding at last the xylenes, then isomerism remains throughout the series of products.

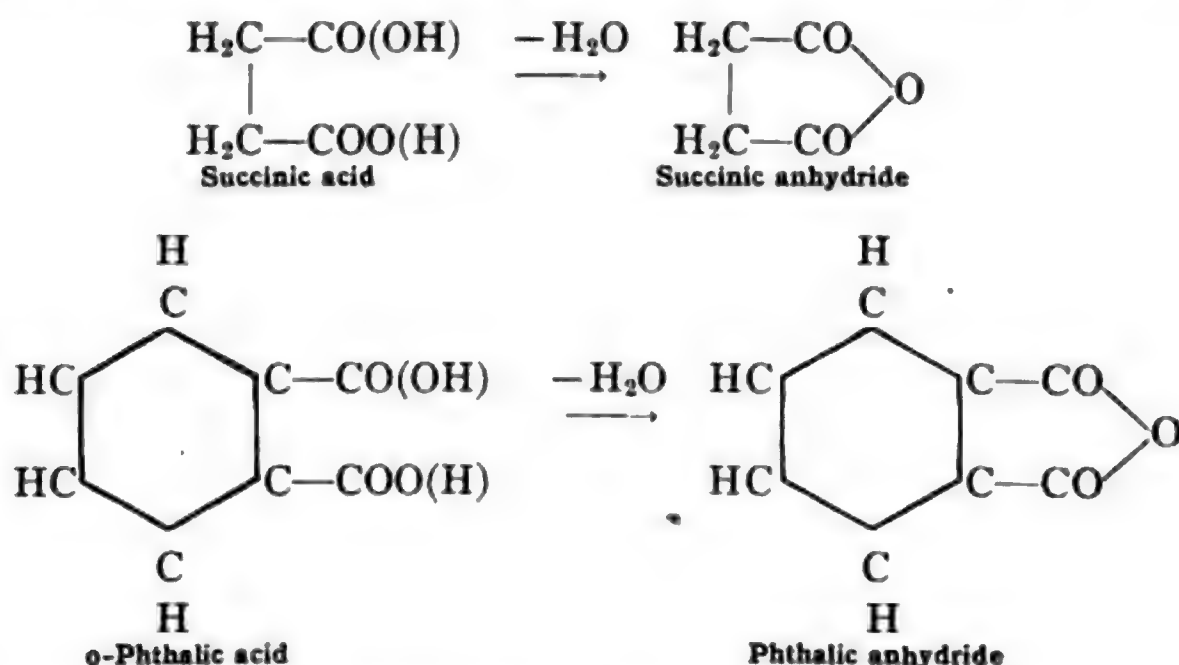
ortho-Phthalic Acid.—The most important of the three acids is the **ortho-phthalic acid** usually termed simply **phthalic acid**. While it may be prepared by the general methods of synthesis the most important method is from **naphthalene**. This method is important both commercially, as in the synthesis of indigo to be discussed later (p. 882), and theoretically in connection with the proof for the constitution of **naphthalene**. The reaction can not be written or explained in detail now, but will be studied later when we consider naphthalene itself (p. 766). When naphthalene, which is a hydrocarbon of a series related to benzene and which has the composition C_{10}H_8 , is treated with chlorine an addition product is formed and then oxidation takes place with the final formation of **ortho-phthalic acid**.



Phthalic acid is a crystalline solid which melts at 184° with the loss of water and the formation of an *anhydride*. It is very slightly soluble in cold water, but quite easily soluble in hot water and in alcohol. The loss of water with the formation of an anhydride is characteristic of the **ortho-phthalic acid** as distinguished from the **meta-** and **para-phthalic acids** which do not yield anhydrides.

Phthalic Anhydride.—In speaking of the formation of anhydrides from the di-basic aliphatic acids, **oxalic acid**, **malonic acid**, **succinic acid**,

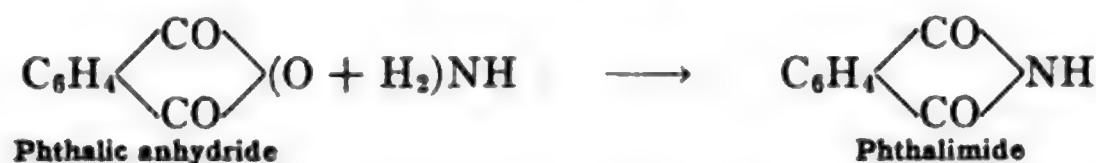
glutaric acid (pp. 281, 287), we found that anhydrides are formed only in the case of those acids in which the carboxyl groups are in close proximity to each other in space, as explained by the tetrahedral carbon atom. Such a condition exists in the cases of succinic acid and glutaric acid, both of which readily form anhydrides, but not in the cases of oxalic and malonic acids, neither of which yield anhydrides. Now if we examine the formula of **ortho-phthalic acid** we shall find that exactly the same space relationship of the two carboxyl groups exists in it as in succinic acid, and in fact both yield anhydrides as follows:



In each case the two carboxyl groups form the ends of a *four carbon* chain and from the tetrahedral models of carbon atoms it will be seen that hydroxyl groups linked to the end carbons of a *four* or *five* carbon chain are in very close proximity. In such cases loss of water takes place easily and an anhydride results. The additional fact that neither **meta-phthalic acid** nor **para-phthalic acid** do form anhydrides strengthens the correctness of the explanation and the truth of the tetrahedral theory. In both of these acids the carboxyl groups are not thus situated in relation to each other, being much further apart, even in the *meta* compound, and they do not lose water. **Phthalic anhydride** is a beautiful crystalline compound forming long white needles, m.p. 128°. When treated with water alone the anhydride is only slightly reconverted into the acid, but when treated with **alkalies** it readily forms salts of the acid. Phthalic anhydride is the most important derivative of the phthalic acids, being of especial importance

in the synthesis of some valuable dyes known as *phthaleins*. When **phthalic anhydride** is heated with **phenol** the common indicator **phenol phthalein** is obtained which is one of the **phthalein dyes**. This and related compounds will be considered later (p. 750).

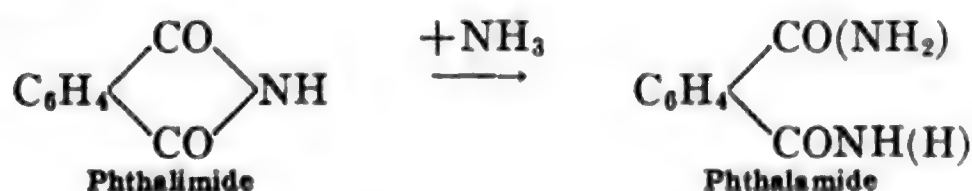
Phthalimide.—Phthalic anhydride also yields other derivatives, viz., **phthalimide** and **phthalyl chloride**. When **phthalic anhydride** is treated with **ammonia** a compound is formed by replacement of the anhydride oxygen with the imide group, ($=\text{NH}$),



This is analogous to the formation of **succinimide** from **succinic anhydride** (p. 284).



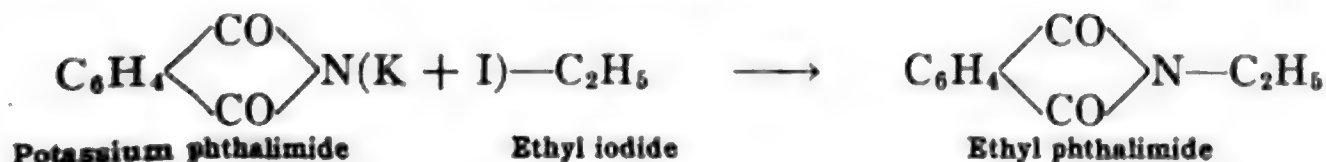
Phthalimide is a crystalline compound which may be sublimed, m.p. 233.5° . With ammonia it yields the *di-amide* of phthalic acid, **phthalamide**.



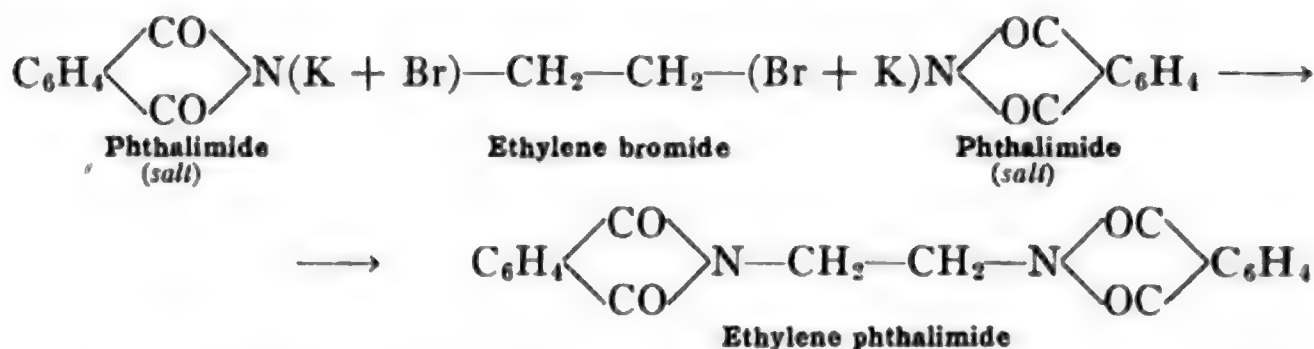
This shows that phthalimide is a compound of an anhydride type formed by loss of ammonia from phthalamide just as phthalic anhydride is formed from phthalic acid by the loss of water. Like other acid amides and imides phthalimide forms salts by replacement of the

imide hydrogen by metals, e.g., potassium phthalimide, $\text{C}_6\text{H}_4 \begin{array}{c} \diagup \text{CO} \diagdown \\ \diagdown \text{CO} \diagup \end{array} \text{NK}$.

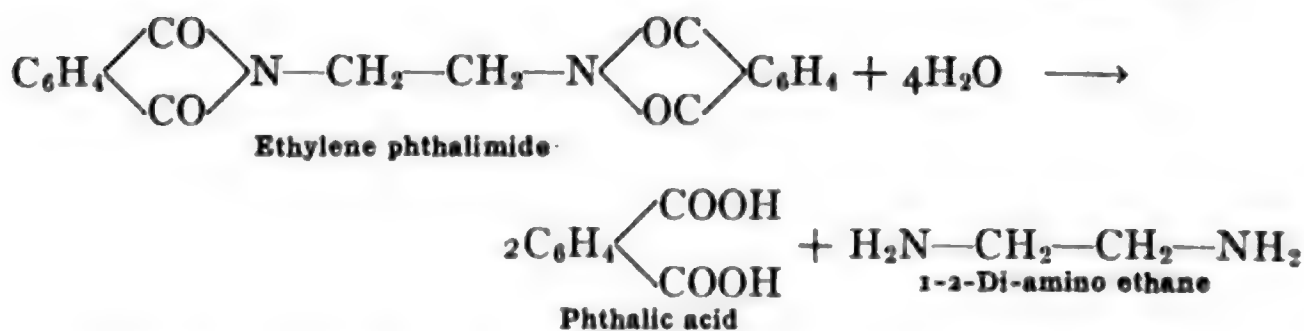
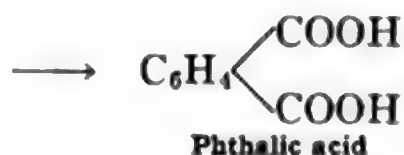
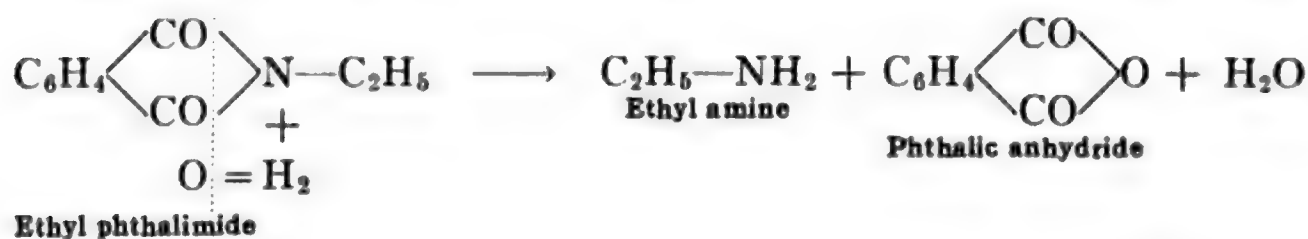
With alkyl halides these salts yield *alkyl phthalimides*.



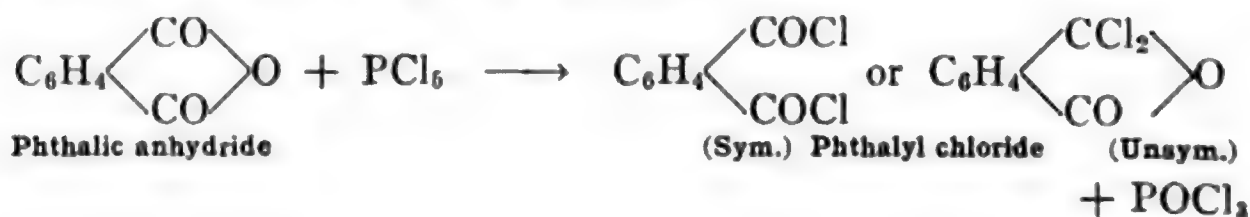
With **ethylene bromide**, **1-2-di-brom ethane**, two molecules of the phthalimide become linked by the ethylene group.



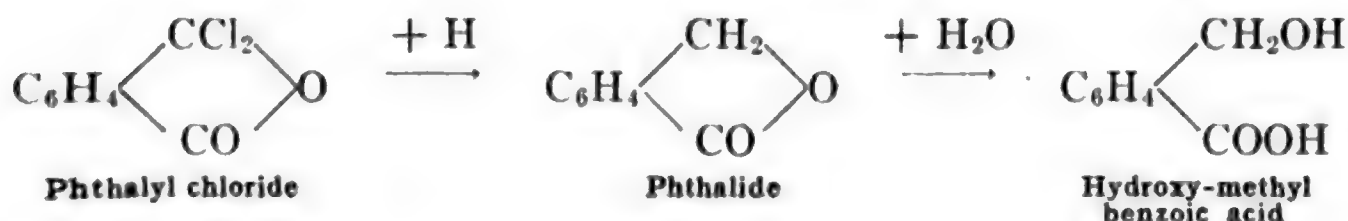
On hydrolysis these compounds split so that the nitrogen remains linked to the aliphatic chain as an aliphatic amine and phthalic acid is re-formed, with phthalic anhydride, probably, as an intermediate step.



Phthalyl Chloride.—When phthalic anhydride is treated with **phosphorus pentachloride**, in the proportion of one molecule of each, two chlorine atoms replace one oxygen atom and a compound is formed known as **phthalyl chloride**, an oily liquid, m.p. 0° , b.p. 275° . Two structures are possible for this chloride.



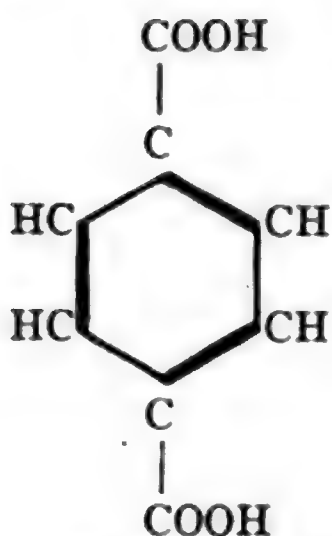
It will be recalled that in the case of **succinyl chloride** both of these forms are obtained, but mostly the symmetrical (p. 282). Now from phthalic anhydride only one phthalyl chloride is obtained. This chloride acts like the *unsymmetrical* succinyl chloride, *not* like the *symmetrical*. The positive proof, however, that **phthalyl chloride** is the *unsymmetrical* compound is the following: Sodium amalgam reduces phthalyl chloride by replacement of the chlorine with hydrogen. The compound formed is known as **phthalide**. This **phthalide** takes up water as anhydrides do and the product is **hydroxy-methyl benzoic acid**.



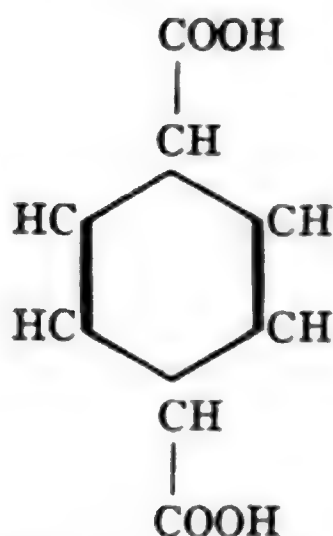
From these relationships it is seen that phthalyl chloride must have the unsymmetrical formula.

meta- and para-Phthalic Acids.—Little need be said in regard to the other two phthalic acids. The *meta* compound, known more commonly as **iso-phthalic acid**, is a solid which crystallizes in needles, m.p. 300°. It sublimes without losing water not yielding an anhydride. It is prepared from **meta-xylene** or from **meta-toluic acid**. The *para* acid, better known as **terre-phthalic acid**, is a crystalline compound which sublimes without melting and without yielding an anhydride. It is prepared from **para-xylene**, **para-toluic acid** or **cymene**, **para-methyl iso-propyl benzene**, also from **turpentine** which is related to cymene (p. 817).

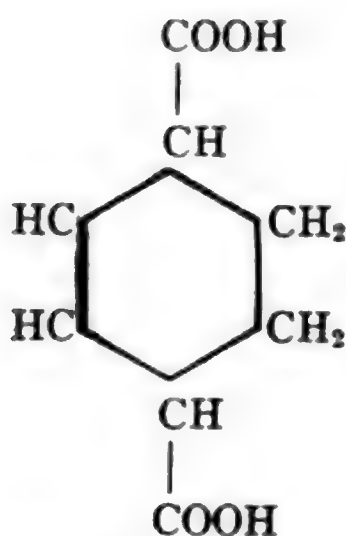
Hydro Phthalic Acids.—An important set of derivatives of the phthalic acids may be mentioned here although they really belong to another series of compounds. These are the **hydro phthalic acids** which are hydrogen addition products. It will be recalled that **benzene** takes up *by addition* either *two*, *four* or *six* **hydrogen** (or bromine) atoms forming **di-hydro benzene**, **tetra-hydro benzene** or **hexa-hydro benzene**, the last being **cyclo-hexane** or **hexa-methylene** (p. 468). For each addition of two hydrogens one of the double bonds of the benzene ring is changed to a single bond. Now the phthalic acids yield an analogous series of hydrogen addition products.



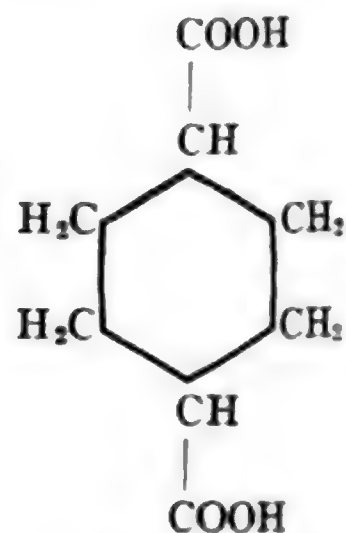
Terre-phthalic acid



Di-hydro terre-phthalic acid

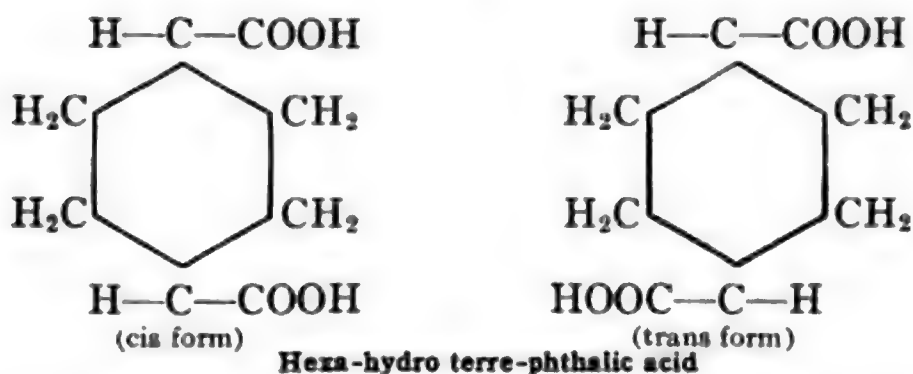


Tetra-hydro terre-phthalic acid



Hexa-hydro terre-phthalic acid

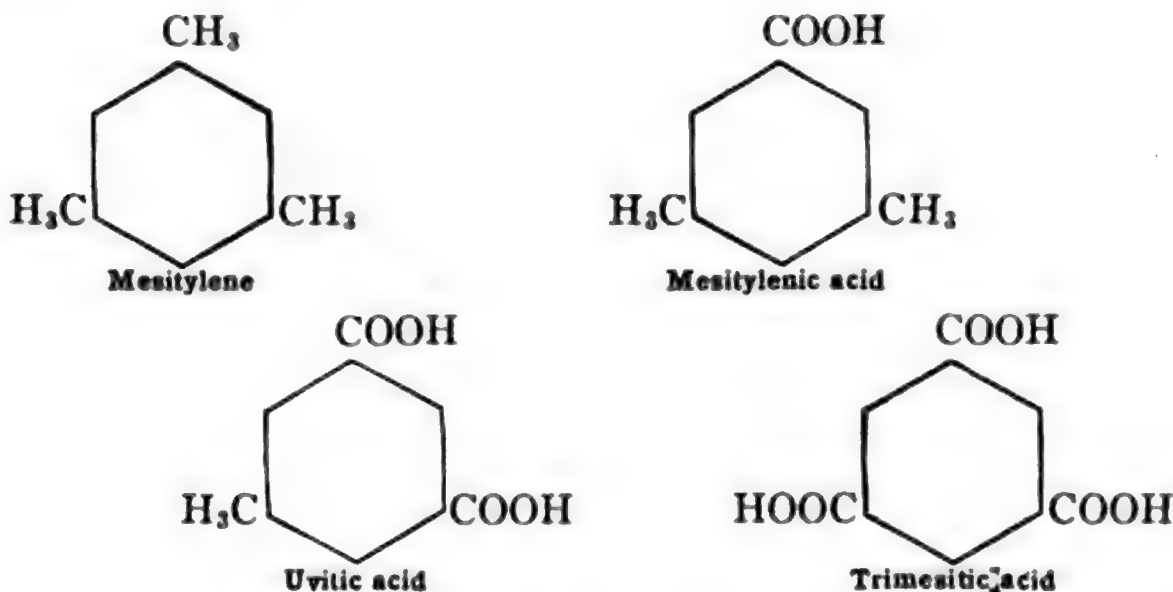
The *hexa-hydro* product is plainly a *di-carboxyl* derivative of **hexamethylene** and thus belongs really to the *poly-methylene* series of compounds and strictly speaking should not be included here as we have said. It will be seen that in the cases of the *di-hydro* and *tetra-hydro* products structural isomerism will occur depending upon the positions, relative to the carboxyl group, which the added hydrogens take, or in other words, the position which the remaining double bonds occupy. This isomerism will be referred to in other connections. In the case of the *hexa-hydro* product all the positions are occupied by an added hydrogen, no double bond remains and, therefore, no *structural isomerism* is possible. The **hexa-hydro terre-phthalic acid**, however, exhibits a case of *stereo-isomerism* of the geometric type as shown in the following formulas:



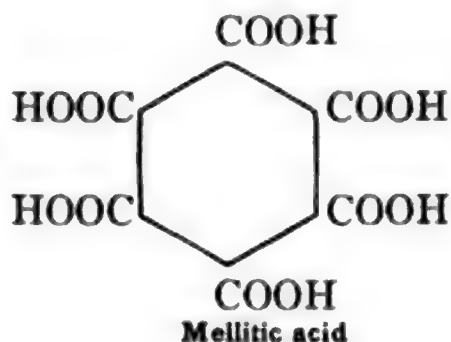
These geometric stereo-isomers are analogous to the similar forms in the case of **maleic acid**, (*cis*), and **fumaric acid**, (*trans*), and take the same distinguishing names.

Uvitic Acid, Tri-mesitic Acid, Mellitic Acid

A few other *poly-basic ring carboxy* acids may be mentioned by name and formula only. Mesitylene, **1-3-5-tri-methyl benzene**, yields a di-carboxy and tri-carboxy acid together with a mono-carboxy acid already referred to.



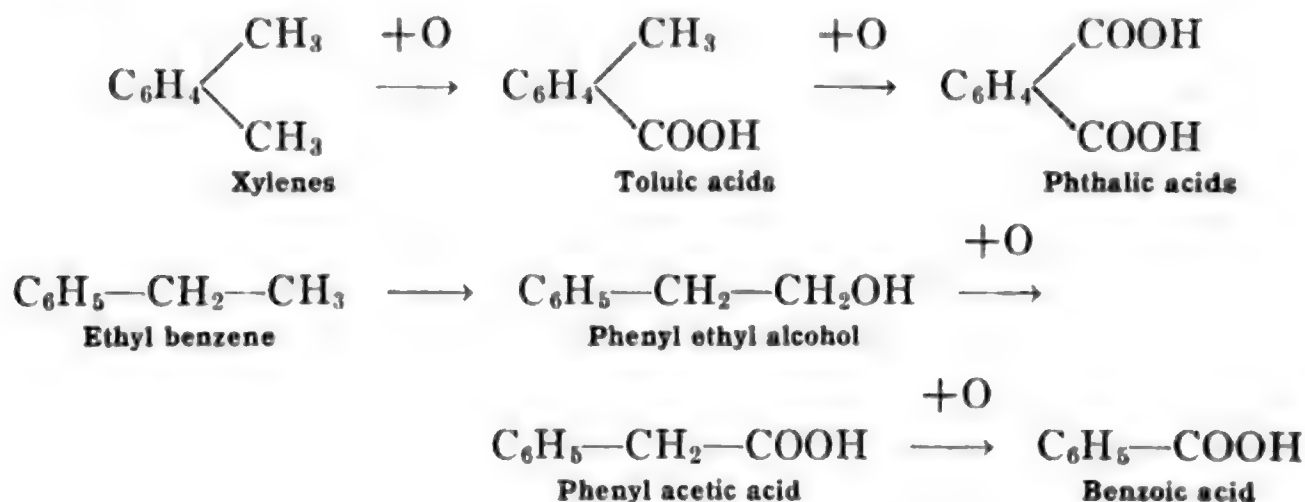
A hexa-carboxy acid is also known, viz., **mellitic acid** or **hexa-carboxy benzene**.



It is found in nature as a mineral, in the form of an aluminium salt known as *honey stone* or *mellite*. It is formed when **graphite** is oxidized with nitric acid and it may be synthesized by oxidizing **hexamethyl benzene**.

Phenyl Acetic Acid, $C_6H_5-CH_2-COOH$, Carboxy-methyl Benzene

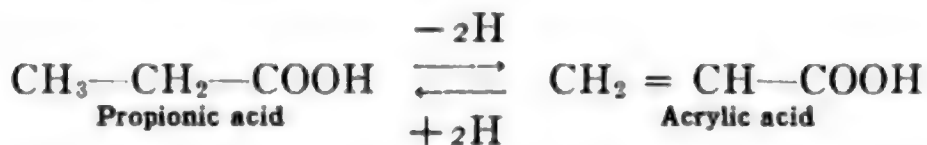
This acid is the simplest aromatic acid with the carboxyl in the side chain. Its name, **phenyl acetic acid**, indicates the relation to the aliphatic acids as a phenyl derivative. The commonly used names for the side-chain carboxy acids are derived similarly, *e.g.*, **phenyl propiolic acid**. It will be seen at once that **phenyl acetic acid** and the **toluic acids** are *isomeric*, the first being the result of the partial oxidation of **ethyl benzene**, the latter the result of the partial oxidation of the **di-methyl benzenes** or **xylenes** which are isomeric with *ethyl benzene*. In both cases the relationship to the hydrocarbon is that only one carbon group of the side chain is oxidized to carboxyl.



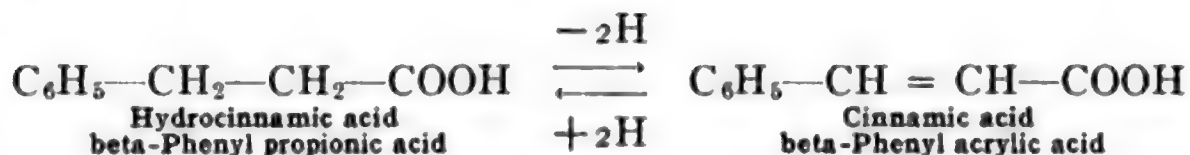
On further oxidation to the final product all the carbon groups of the side chain are completely oxidized and the products are as above, the **dimethyl benzenes** and **toluic acids** yielding *di-carboxyl* ring acids while **ethyl benzene** and **phenyl acetic acid** yield the mono-carboxyl ring acid. This relationship shows clearly the difference in character between a *ring carboxyl* acid and an isomeric *side-chain carboxyl acid*. Because of its isomerism with toluic acid phenyl acetic acid is also known as **alpha-toluic acid**, a name that does not seem advisable. While phenyl acetic acid is not of especial importance, the other side-chain carboxyl acids which we shall mention are of considerable importance.

Hydrocinnamic Acid and Cinnamic Acid

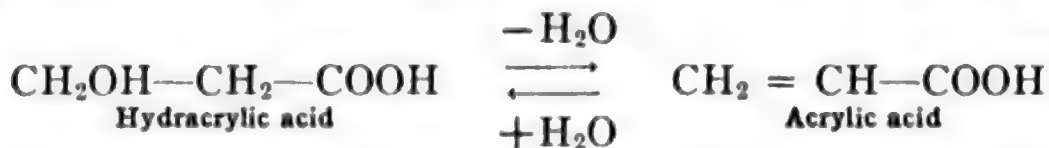
The next higher homologous side-chain carboxyl acid is the one in which the side chain has three carbon groups, $\text{C}_6\text{H}_5\text{—CH}_2\text{—CH}_2\text{—COOH}$. It is, therefore, **beta-phenyl propionic acid** or **1-carboxy 2-phenyl ethane**. It is commonly known as **hydrocinnamic acid** because of its relation to **cinnamic acid** as the hydrogenated or reduction product. In the aliphatic series we have two acids, one, **propanoic acid** or **propionic acid**, the other **propenoic acid** or **acrylic acid**. They are related to each other as corresponding saturated and unsaturated compounds (p. 172). The latter, **acrylic acid**, yields propionic acid on reduction by the addition of two hydrogen atoms and the conversion of the unsaturated chain into a saturated one.



Now **hydrocinnamic acid** bears exactly the same relationship to **cinnamic acid**, the former being **phenyl propionic acid**, the latter **phenyl acrylic acid**.



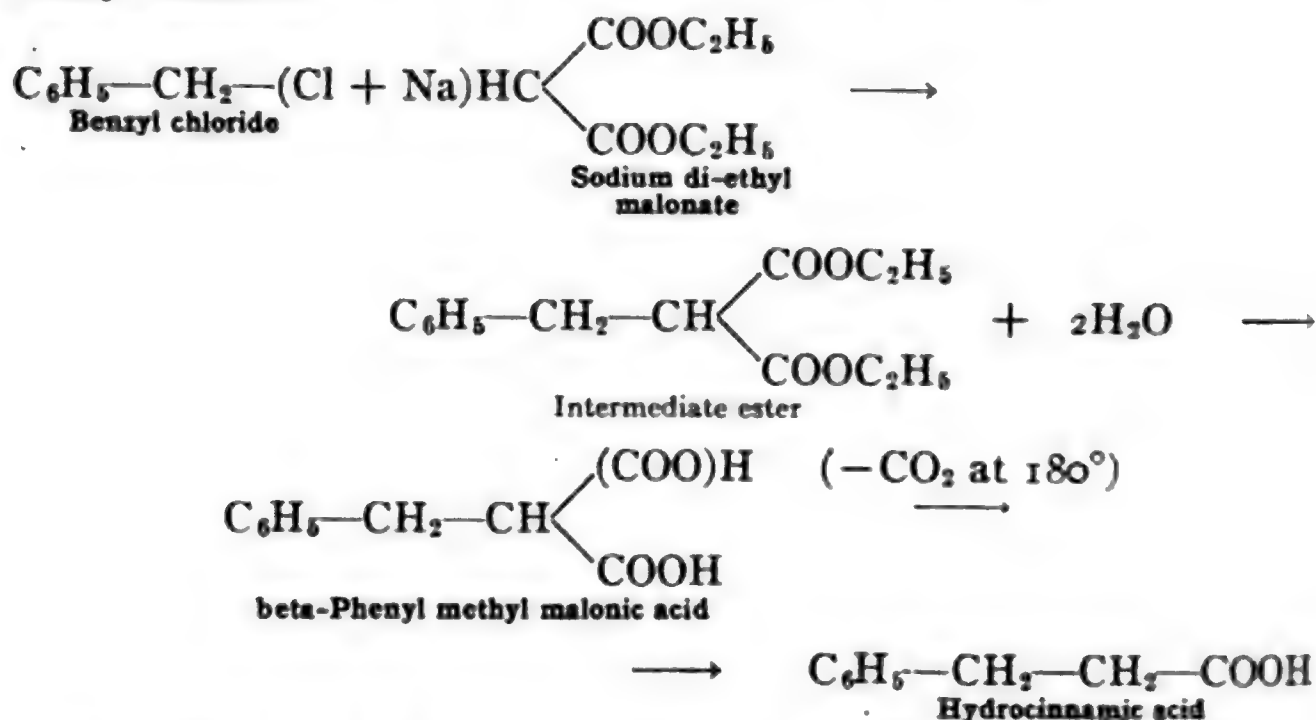
It may be well to mention here another acid already discussed, the name of which indicates a similar and yet distinctly different relationship from that indicated by the name hydrocinnamic acid. This acid is **hydracrylic acid** (p. 245). It is related to **acrylic acid** as follows:



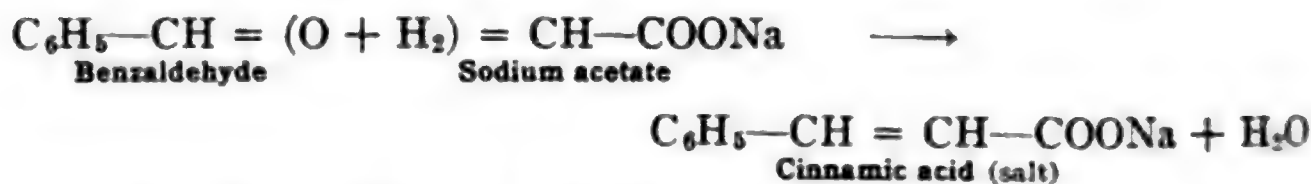
Here the relationship is that of loss or addition of water, the name *hydr-acrylic* meaning *hydrated acrylic*, whereas the relationship between **cinnamic acid** and **hydrocinnamic** is loss or addition of **hydrogen**, the name hydro-cinnamic meaning *hydrogenated cinnamic*. The same relationship is expressed in the case of propionic acid if we name it **hydro-acrylic acid**.

Malonic Ester Synthesis of Hydrocinnamic Acid.—While hydrocinnamic acid is usually prepared by the reduction of cinnamic acid it

may also be prepared by the **malonic ester synthesis** (p. 274) from **benzyl chloride**.



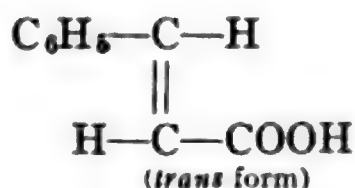
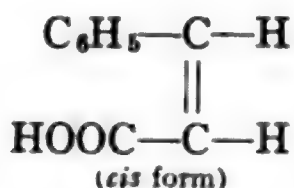
Cinnamic Acid by Perkin's Reaction.—Cinnamic acid has the constitution assigned to it above as is proven by the following synthesis from **benzaldehyde** by *condensation* with **sodium acetate** in the presence of acetic anhydride.



The reaction is known as **Perkin's reaction** and is applicable to the preparation of any unsaturated acid, and is especially used in the benzene series. By using salts of different aliphatic acids in place of acetic acid any desired product may be obtained. The aldehyde may also be varied, but the aldehyde group must be linked to the ring. Also in case of aliphatic acids containing several carbon groups the condensation of the aldehyde always takes place with the carbon group, $(\text{CH}_2)_n$, which is linked to the carboxyl. The reaction probably takes place like the *aldol* condensation (p. 116), yielding a hydroxy acid as an intermediate product, which then loses water, yielding the unsaturated acid.

Isomerism.—Cinnamic acid occurs as geometric stereo-isomers, *i.e.*, as *cis* and *trans* forms like **maleic** and **fumaric acids** (p. 291) and **crotonic** and **iso-crotonic acids** (p. 177). This is apparent as it is

the *phenyl* analogue of crotonic acid, cinnamic acid being *beta-phenyl* acrylic acid and crotonic acid *beta-methyl* acrylic acid. The two forms are as follows:



Cinnamic and Allo-cinnamic acids

Which of the two is the *cis* form and which the *trans* form has not been determined. A third cinnamic acid, viz., **iso-cinnamic** acid, is also known, but the constitution of it has not been established. Cinnamic acid is found in nature in the resin *storax* both as the free acid and as the cinnamic alcohol ester, **styrin**. It is also found in *Peru* and *Tolu balsams* as the free acid and as the benzyl alcohol ester, the benzoic acid ester of benzyl alcohol being present also. Thus benzyl alcohol, benzoic acid, cinnamic alcohol and cinnamic acid are all constituents of esters present in these plant resins. **Allo-cinnamic** acid, the geometric isomer, is obtained from *coca* leaves from which the alkaloid **cocaine** is also obtained (p. 896). When cinnamic acid is heated with lime it loses carbon dioxide and yields the unsaturated side-chain hydrocarbon **styrene**, or phenyl ethylene, $\text{C}_6\text{H}_5-\text{CH}=\text{CH}_2$. On reduction it yields first **cinnamic aldehyde**, found in *oil of cinnamon* (p. 842) and then **cinnamic alcohol**. Both cinnamic acid and allo-cinnamic acid yield anhydrides.

Atropic Acid.—A structural isomer of cinnamic acid is an acid obtained by loss of water from **tropic acid** and, therefore, known as **atropic acid**. It has been shown to be the *alpha* isomer of cinnamic acid, i.e., **alpha-phenyl acrylic acid**, $\text{C}_6\text{H}_5-\text{C}=\text{CH}_2$. Tropic acid is a



constituent of the alkaloid **atropine** which is related to cocaine, the alkaloid of *coca* leaves, which also yields allo-cinnamic acid. Such facts in regard to the natural occurrence of related compounds are of great interest and undoubtedly of special biological significance of which only little is yet known. The alkaloids referred to will be studied later (p. 886).

Other Unsaturated Side-chain Carboxy Acids

Phenyl Crotonic Acid. Phenyl Vinyl Acetic Acid.—A phenyl derivative of crotonic acid is known, $\text{C}_6\text{H}_5\text{—CH}_2\text{—CH}=\text{CH—COOH}$, **beta-benzyl acrylic acid**. Also the structural isomer of crotonic acid, viz., **vinyl acetic acid**, $\text{CH}_2=\text{CH—CH}_2\text{—COOH}$, yields a phenyl derivative, $\text{C}_6\text{H}_5\text{—CH}=\text{CH—CH}_2\text{—COOH}$, **phenyl vinyl acetic acid** or **1-phenyl Δ_1 -butenoic-4 acid**, which is important in connection with the constitution of naphthalene (p. 768).

Phenyl Propiolic Acid.—The acetylene unsaturated side chain hydrocarbon phenyl propine, $\text{C}_6\text{H}_5\text{—C}\equiv\text{C—CH}_3$, yields an acid known as **phenyl propiolic acid**, $\text{C}_6\text{H}_5\text{—C}\equiv\text{C—COOH}$, which by loss of carbon dioxide yields phenyl acetylene, $\text{C}_6\text{H}_5\text{—C}\equiv\text{CH}$. The acid is important in connection with the synthesis of indigo (p. 879).

X. SUBSTITUTED AROMATIC ACIDS

The different kinds of substitution products of the aromatic acids which it is possible to obtain are very numerous. Without reference to the particular element or group which is substituted we may have the following types.

Ring carboxy acids:

Substitution in the *ring*, e.g., $\text{C}_6\text{H}_4 \begin{matrix} \text{COOH} \\ \text{I} \end{matrix}$ **Iodo benzoic acid**

Substitution in the *side chain*, e.g., $\text{C}_6\text{H}_4 \begin{matrix} \text{COOH} \\ \text{CH}_2\text{OH} \end{matrix}$ **Hydroxy-methyl benzoic acid**

Side-chain carboxy acids:

Substitution in the *ring*, e.g., $\text{C}_6\text{H}_4 \begin{matrix} \text{CH}=\text{CH}-\text{COOH} \\ \text{NO}_2 \end{matrix}$ **Nitro cinnamic acid**

Substitution in the *side chain*, e.g., $\text{C}_6\text{H}_5-\text{CH}_2-\text{CH}(\text{NH}_2)-\text{COOH}$ **Phenyl alanine**

Substitution in the *ring and side chain*, e.g., $\text{C}_6\text{H}_4 \begin{matrix} \text{CH}_2-\text{CH}(\text{NH}_2)-\text{COOH} \\ \text{OH} \end{matrix}$ **Tyrosine**

Mixed ring-carboxy and side-chain carboxy acids:

$\text{C}_6\text{H}_4 \begin{matrix} \text{COOH} \\ \text{NH}-\text{CH}_2-\text{COOH} \end{matrix}$ **Phenyl glycine
o-carboxylic acid**

The general methods of synthesis of all these types are two: (1) From the acid itself by direct substitution of the desired element or group into ring or side chain. This method will vary according to whether the substitution is in the ring or side chain, and whether the side chain is saturated or unsaturated. (2) From a substituted *hydrocarbon*, *nitrile*, *amine*, etc., and the conversion of this into the acid by one of the methods already discussed under the synthesis of acids.

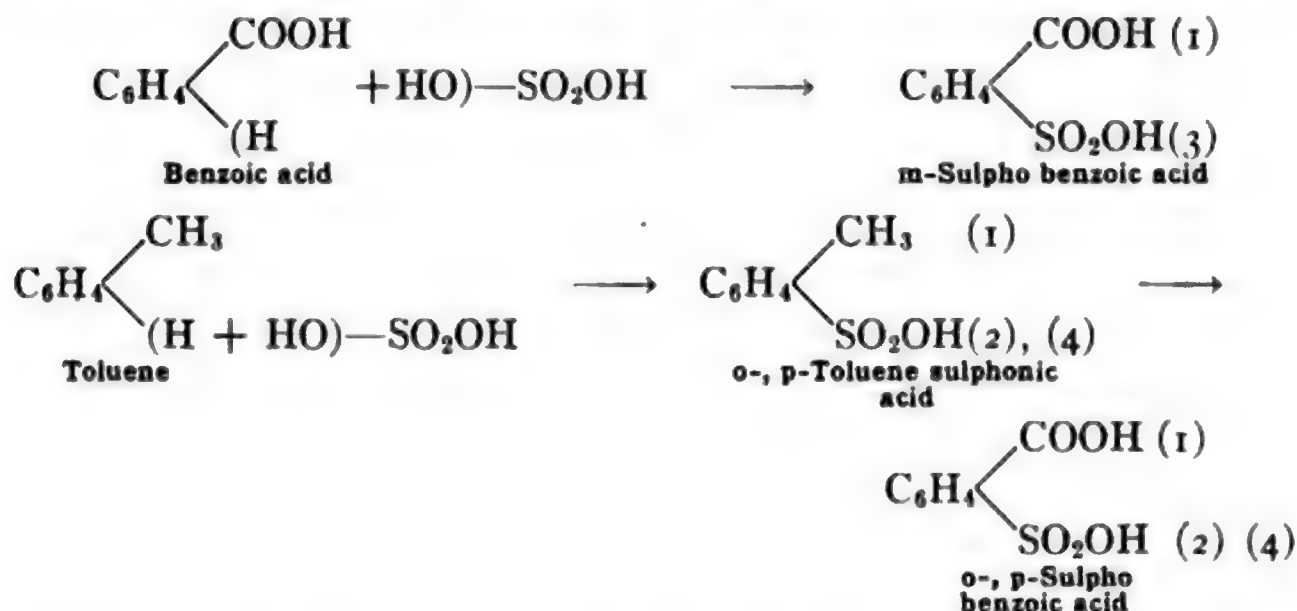
While the known compounds representing the various types are many only a relatively few will be considered individually. These will include those which are important in themselves or that are related to other important compounds which have already been studied or that will be studied later. Some members of the class not mentioned now may be referred to later, in their proper connection in relation to some important product. At the outset in considering a large class such as the one which we are discussing it is well to make a survey of the theoretical possibilities for they are not simply theoretical possibilities but have become actual facts established by the study of definite compounds.

RING SUBSTITUTED RING CARBOXY ACIDS

Let us now examine the conditions to be met in applying either of the two general methods just given to the formation of a substituted ring-carboxy acid in which the substitution also is to be in the ring.

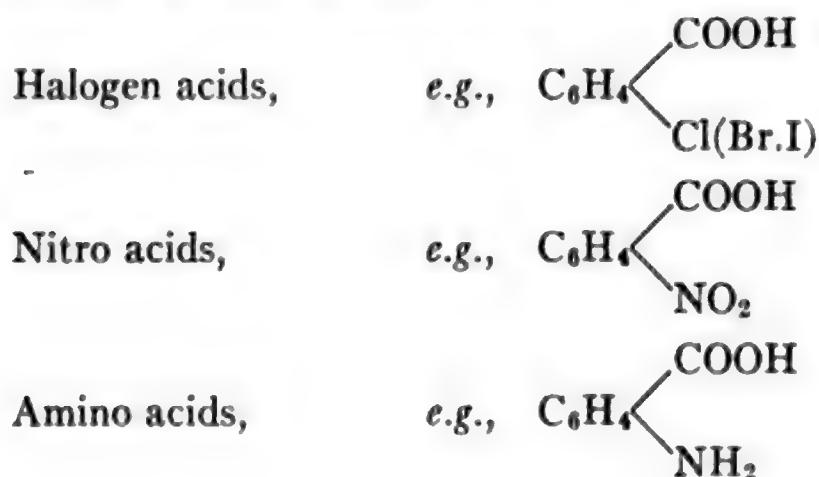
Influence of Carboxyl.—The first condition is that the presence of a *carboxyl group in the ring* has a decided influence on the further ring-substitution of the compound. We have stated before that in general the presence of an element or group in the benzene ring makes the introduction of a second one much more easy. Benzoic acid, therefore, just like toluene, is more easily nitrated or sulphonated, for example, than is benzene. The presence of the carboxyl group also determines the position which a second substituting group usually enters. We have given the following as the general rule (p. 506). When a benzene ring has already substituted in it a halogen element, (Cl., Br), an amino, ($-\text{NH}_2$), hydroxyl, (OH), or methyl, (CH_3), group then a second element or group substituted by direct action usually enters both the *para* and *ortho* positions, the former usually in larger amount, but not the *meta*. On the other hand, when the original substituted group is an *aldehyde*, ($-\text{CHO}$), *carboxyl*, ($-\text{COOH}$), *cyanogen*, ($-\text{CN}$), *nitro*, ($-\text{NO}_2$), or *sulphonic acid*, ($-\text{SO}_2\text{OH}$), group then a second element or group substituted by direct action usually enters the *meta* position. Therefore when a substituted acid is made by direct substitution of a ring-carboxy acid itself we usually obtain the *meta* compound. In order to prepare the *ortho* and *para* compounds we must use the second general method of indirect substitution, viz., starting with a hydrocar-

bon, phenol or amine, we introduce the desired group and then convert the substituted compounds, which will be the *ortho* and *para*, into the acid by appropriate reactions. This may be illustrated as follows:



As both nitration and sulphonation take place with comparative ease, with either hydrocarbons or acids, and as the *nitro* compounds yield *amino* compounds and these yield *diazo* compounds, with their numerous reactions, in particular the **Sandmeyer** reaction for obtaining nitriles; and as *sulphonic* acids are easily converted into *phenols* or *nitriles*; it will be seen that by a combination of these synthetic reactions practically any desired ring-substituted mono-basic or poly-basic ring-carboxy acid may be obtained.

Classified according to the character of the substituting element or group the substituted aromatic acids may be put in the following classes, embracing all of the types previously given with one exception. Taking for illustration the ring-substituted ring-carboxy acids and using benzoic acid as our example we have:



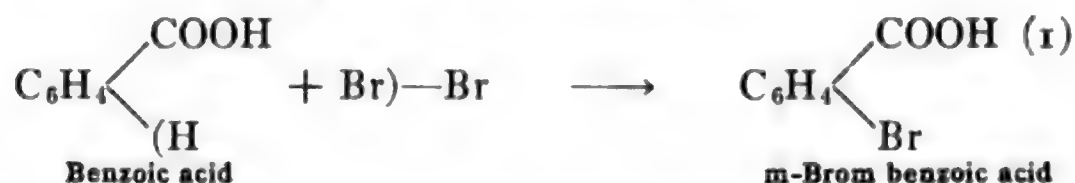
Sulpho acids, (mixed *e.g.*, $\text{C}_6\text{H}_4 \begin{cases} \text{COOH} \\ \text{SO}_2\text{OH} \end{cases}$
sulphonic acids and
carboxy acids)

Hydroxy acids, *e.g.*, $\text{C}_6\text{H}_4 \begin{cases} \text{COOH} \\ \text{OH} \end{cases}$

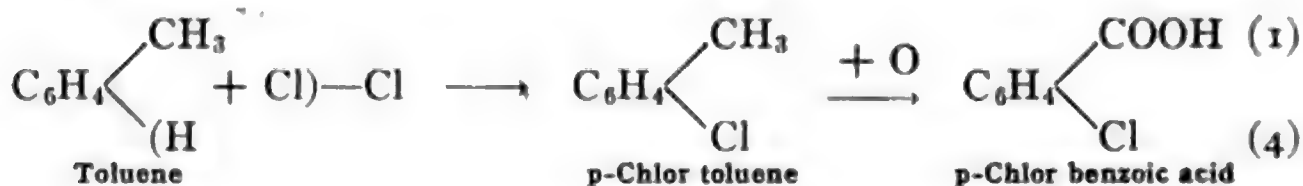
The last three are by far the most important.

HALOGEN AROMATIC ACIDS

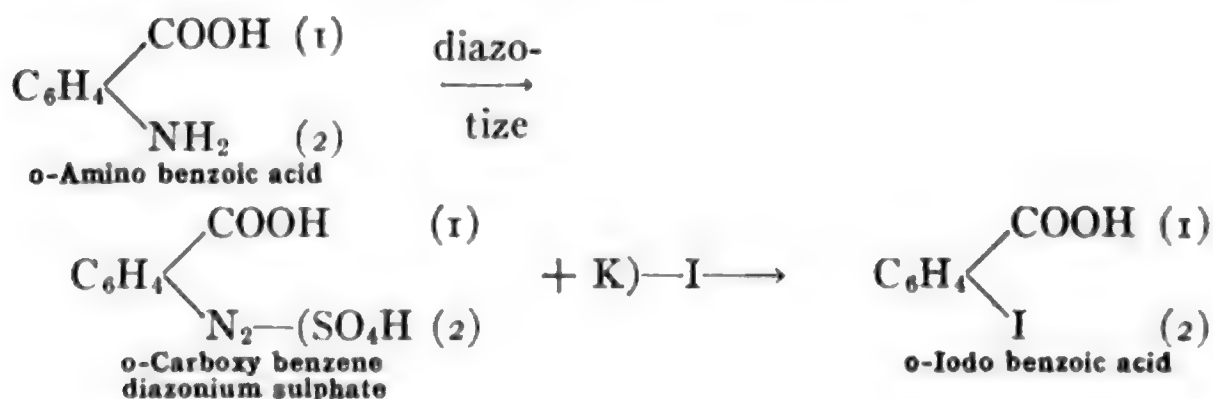
The halogen ring-substituted acids are prepared by some one of the general methods of synthesis, depending on whether the desired product is the *ortho*, *meta* or *para* compound. The *meta* acids are made by direct action of a halogen on the aromatic acid.



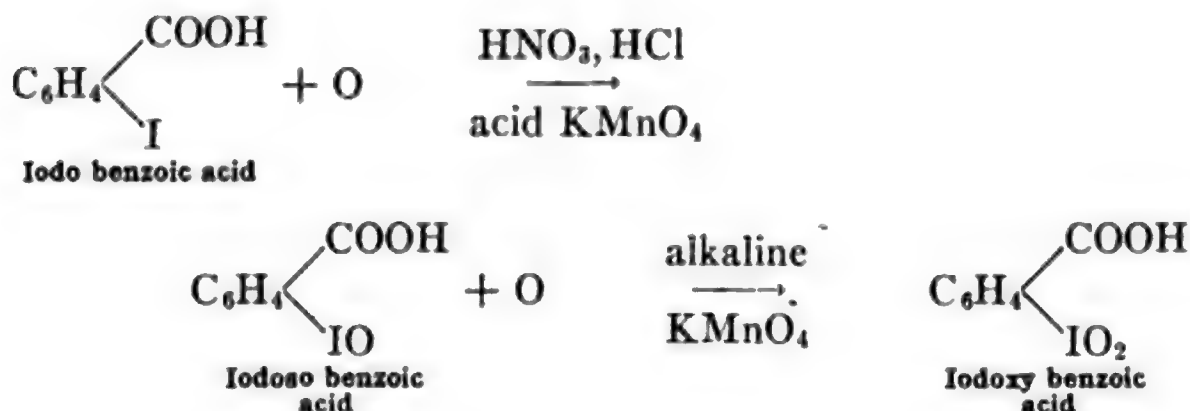
The *para* acids are usually made by halogenating a hydrocarbon and then oxidizing the side chain to carboxyl.



The *ortho* compound, while obtained in small amounts by the above reaction, is better prepared from the *ortho amino acid* by the *diazo reaction* and replacement of the diazo group with a halogen by the **Sandemeyer reaction** or by means of potassium iodide (p. 598).

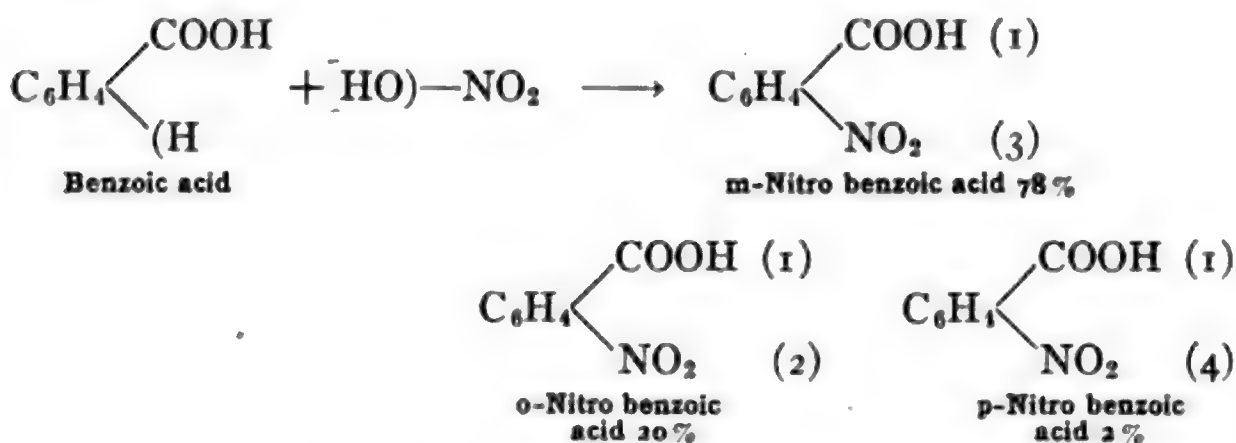


ortho-Iodo Benzoic Acid.—The *ortho*-iodo benzoic acid just given in the last synthesis is important historically because it was the first iodine compound to yield *iodoso* and *iodoxy* derivatives (p. 508) as follows:



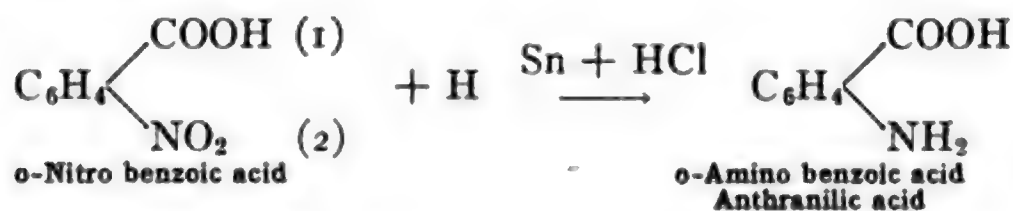
NITRO AND AMINO AROMATIC ACIDS

Nitro Benzoic Acids.—The nitro ring-substituted acids are not in themselves of special importance, but on reduction they yield the corresponding amino acids which have many important members. The two groups may thus be considered together. When direct nitration of the aromatic acid is carried out by treatment with nitric acid or a mixture of nitric and sulphuric acids the chief product is the *meta* compound. In the case of benzoic acid the yield of isomeric products is about as follows:

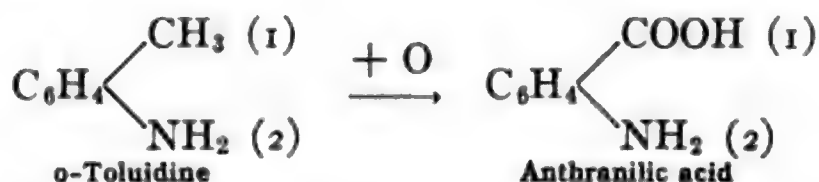


Anthranilic Acid.—Nitration of toluene and subsequent oxidation yields largely the *para* and *ortho* compounds. A fact of interest in connection with these **nitro benzoic acids** is that the *ortho* acid is *sweet* while the *meta* and *para* acids are *bitter*. On reduction with tin and

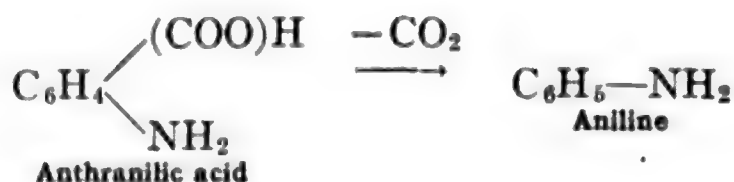
hydrochloric acid the nitro benzoic acids yield the corresponding amino benzoic acids.



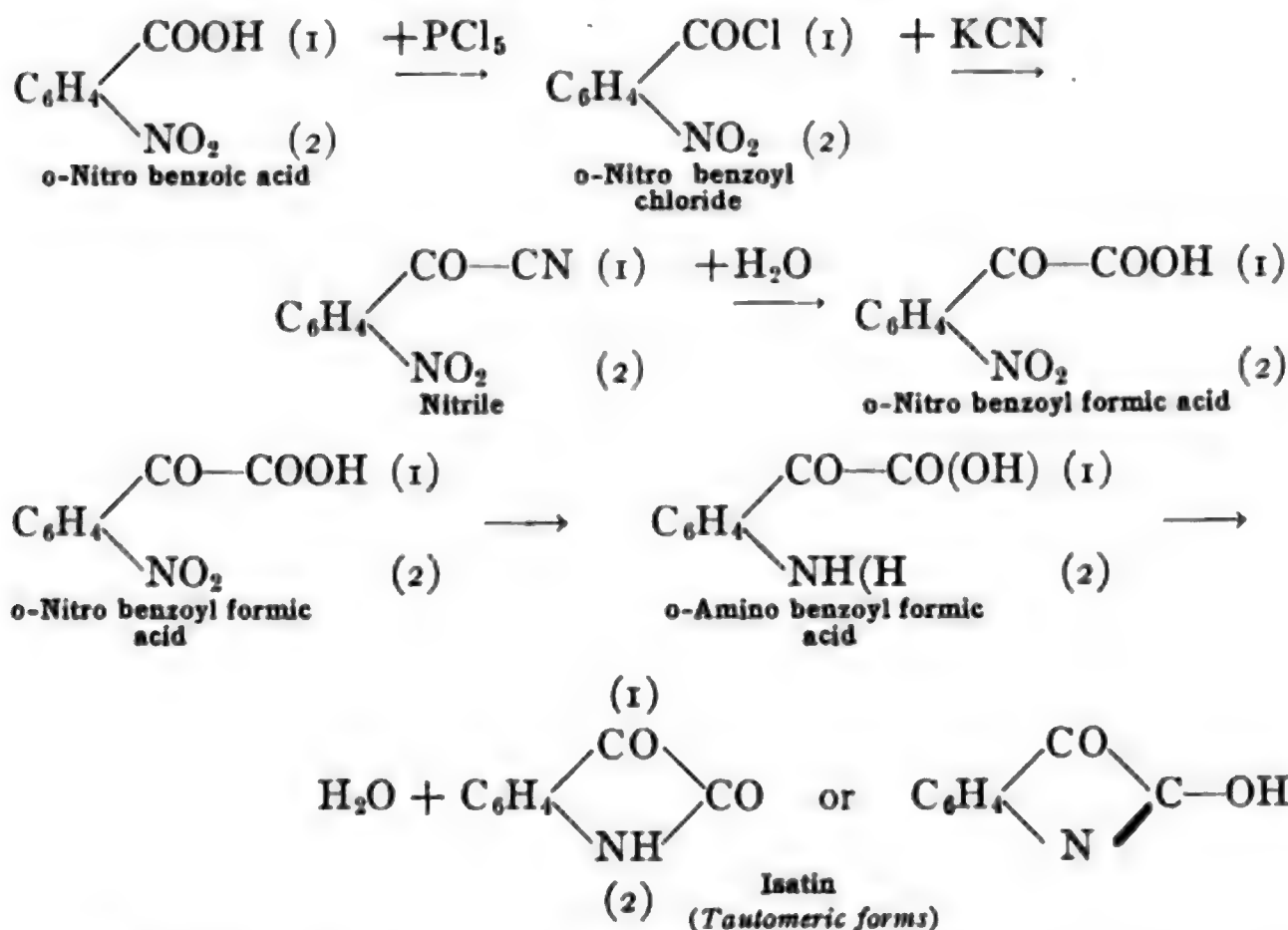
The **ortho-amino benzoic acid** is known also as **anthranilic acid** and is the most important of the amino benzoic acids. In addition to the above synthesis, the **ortho-nitro benzoic acid** being prepared from **ortho-nitro toluene** by oxidation, the amino acid may also be made by converting the **ortho-nitro toluene** into **ortho-amino toluene** or **ortho-toluidine**, the latter being also a natural product of coal tar distillation and a constituent of *crude aniline* made from unpurified benzene through the nitro compound (p. 544). **ortho-Toluidine** on oxidation yields the **anthranilic acid**.



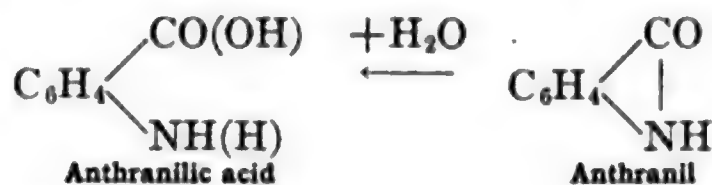
Relation to Indigo.—These syntheses while establishing the constitution of **anthranilic acid** as **ortho-amino benzoic acid** are not the most important. The extreme importance of this particular amino acid is in its connection with the synthesis of the valuable dye **indigo**. The relation of the acid to indigo involves several other compounds which must be mentioned. The Portuguese name for indigo, viz., *anil*, has given us the name for *anil*-ine which, as stated before (p. 539), is obtained when indigo is distilled with alkali. It also gives us the name *anthr-anil*-ic acid, for this acid is obtained from indigo on fusion with alkali. That it is an intermediate product in the breaking down of indigo to aniline is shown by the fact that it yields aniline by the loss of carbon dioxide just as benzoic acid yields benzene.



Isatin.—Another compound is also obtained on the oxidation of indigo, viz., **isatin**. That isatin is related to anthranilic acid and is probably another intermediate product of the breaking down of indigo, lying between indigo and anthranilic acid, may be seen by the following synthesis of isatin from **ortho-nitro benzoic acid**.

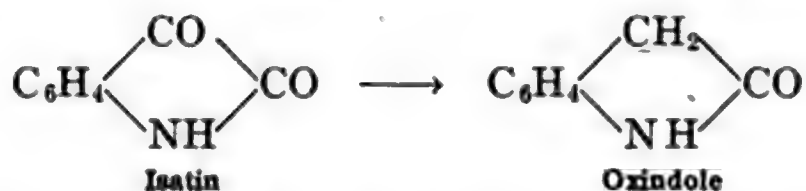


Anthranil.—The same characteristic anhydride linkage between the *ortho* carboxyl and amino groups is found in another compound that, because of its relation to anthranilic acid, which it yields by addition of water when heated with sodium hydroxide solution, is known as **anthranil**. It is related to anthranilic acid as an *inner anhydride*.



Such anhydride relation between *ortho* groups, from which water may be lost, has been found before in the cases of **phthalic anhydride** (p. 689), **phthalimide** (p. 691), and succinic anhydride and **succinimide** (p. 280–283).

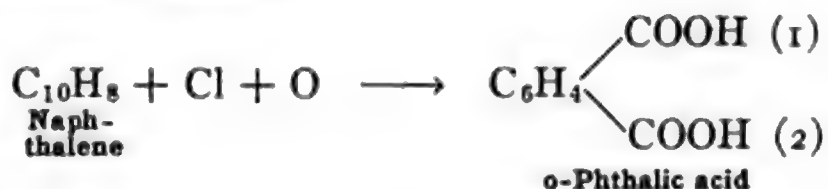
Oxindole.—Still one more related compound should be mentioned. This is **oxindole** which is a reduction product of **isatin**.



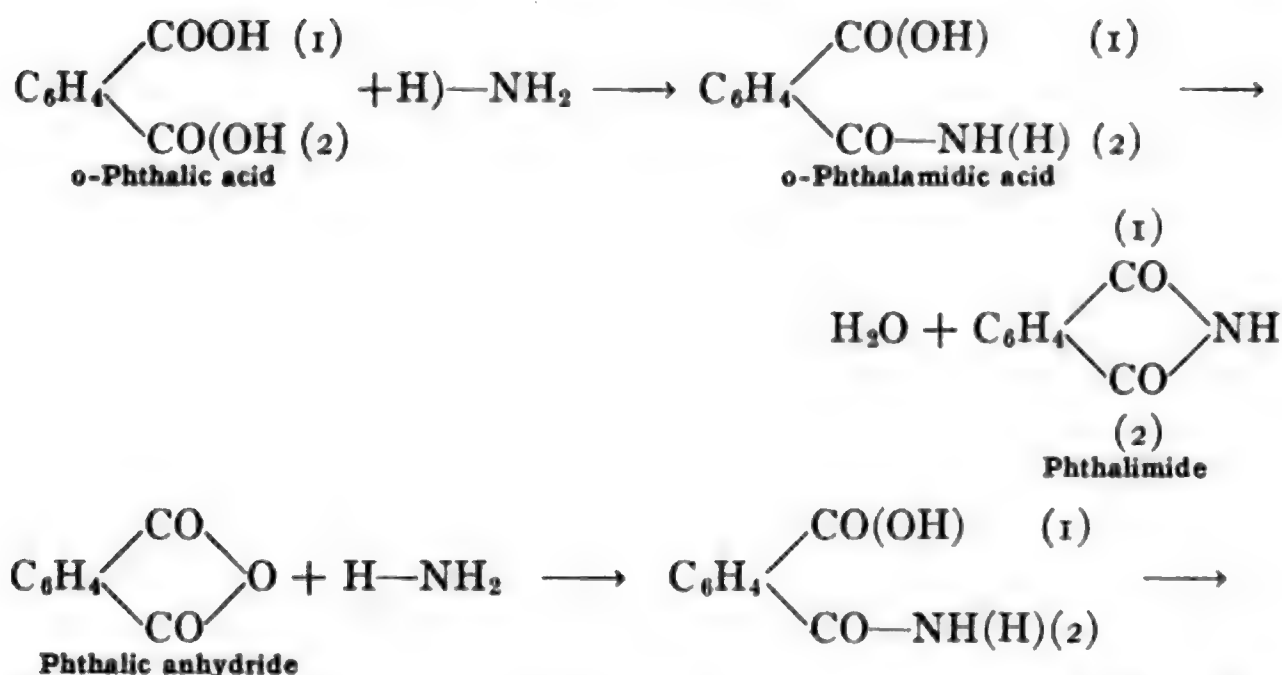
All of these compounds which we have given as related to anthranilic acid and to indigo are plainly derivatives of *ortho-amino* aromatic acids, either benzoic acid itself, as in anthranilic acid and anthranil, or side-chain-carboxy acids, as in isatin and oxindole.

Synthesis of Anthranilic Acid and Indigo.—While anthranilic acid was first obtained from indigo the importance of the acid now is due to the fact that it is an intermediate step in the *synthesis of indigo*. It was through a study of the relationships which we have just been discussing that a commercial method for the synthesis of this valuable dye was worked out. Anthranilic acid may be converted into indigo by a reaction which we shall not discuss in detail until indigo itself is studied. To make such a synthesis of indigo successful it was necessary, however, to secure other methods than those given for synthesizing the acid and especially to have as the starting point a cheap commercial compound.

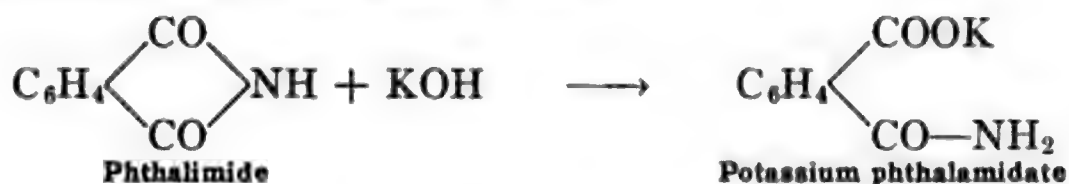
Synthesis from Phthalic Acid and Naphthalene.—This was found when anthranilic acid was synthesized from **ortho-phthalic acid** which, as has been stated, may in turn be synthesized from **naphthalene**, a cheap abundant compound. The conversion of naphthalene into *ortho-phthalic acid* we have given (p. 689) as resulting from chlorination and subsequent oxidation.



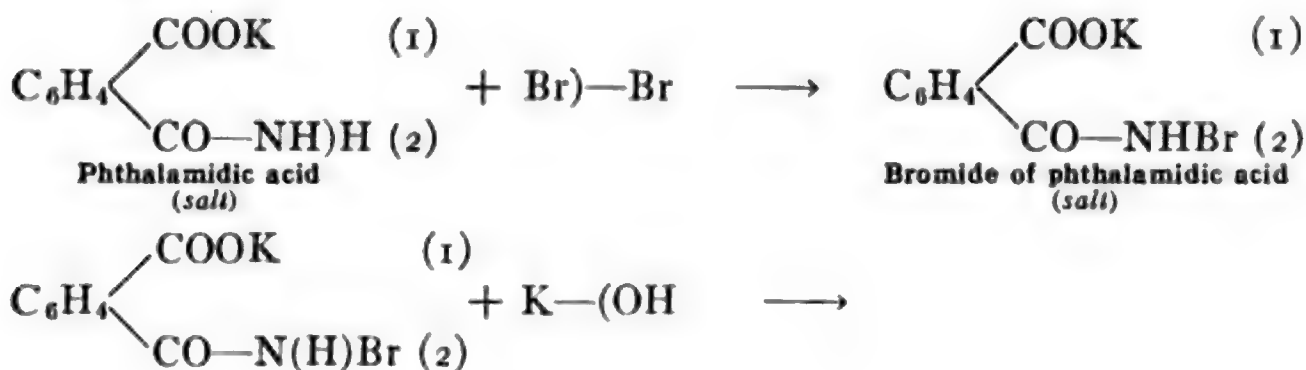
The details of this synthesis will be explained under naphthalene (p. 766). The synthesis of anthranilic acid from *ortho-phthalic acid* takes place according to the following reactions. Phthalic acid, or better **phthalic anhydride**, by treatment with ammonia yields **phthalamidic acid**, which in turn yields **phthalimide**.

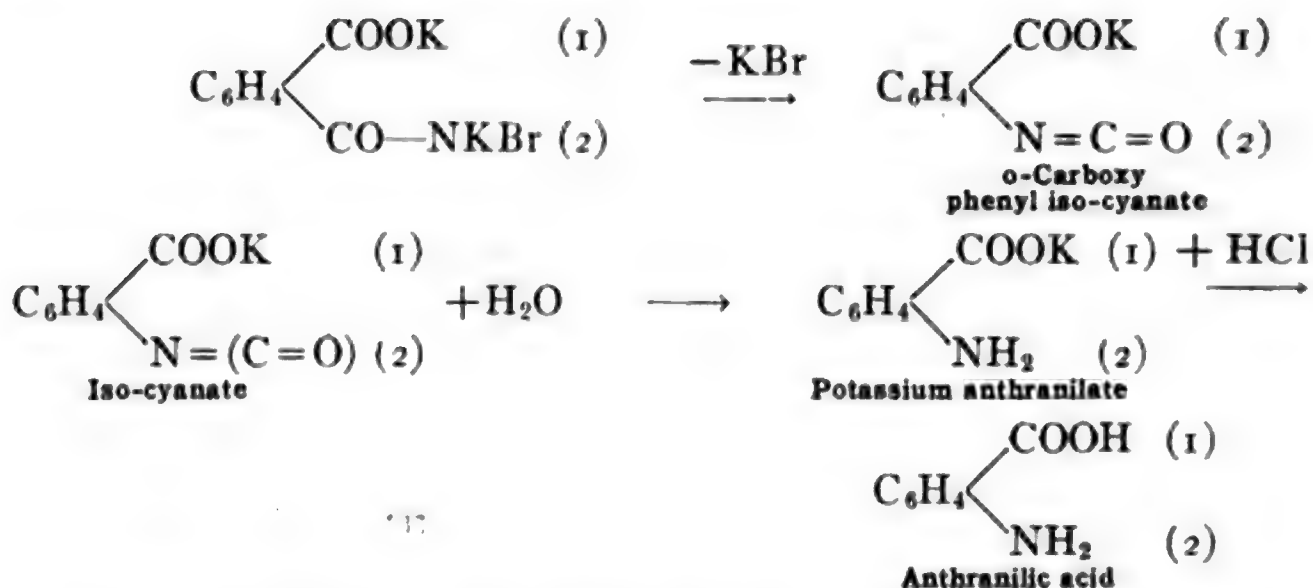


The reaction is accomplished by simply heating together **phthalic anhydride** and **ammonium carbonate**. Phthalimide then hydrolyzes with potassium hydroxide yielding the potassium salt of phthalamidic acid and this acid amide compound undergoes the **Hofmann reaction** (pp. 148, 685) with bromine (or chlorine) and potassium hydroxide by which one of the carboxyl groups is replaced by the amino group yielding amino benzoic acid or **anthranilic acid**.

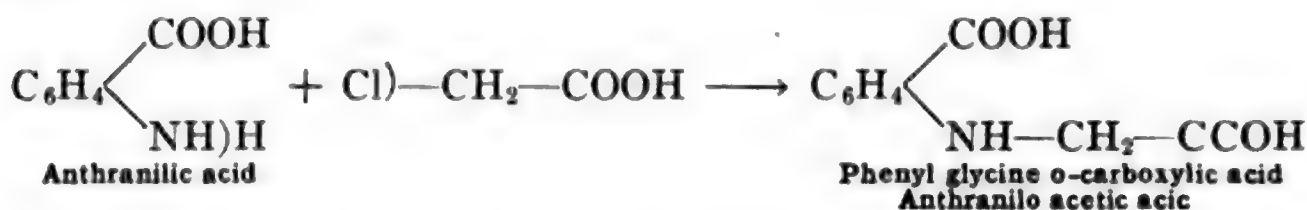


Hofmann Reaction.—In the reaction with phthalic acid or anhydride and ammonia the phthalamidic acid may be isolated without going on to phthalimide. In this case the action of potassium hydroxide is simply neutralization and formation of the above salt. The **Hofmann reaction** with phthalamidic acid may be represented in steps as follows:





Phenyl Glycine ortho-Carboxylic Acid.—The next step toward indigo is the formation of **phenyl glycine ortho-carboxylic acid** which is an *ortho*-amino derivative of a mixed ring-carboxy and side-chain-carboxy acid. With **chlor acetic acid** anthranilic acid forms an amino acetic acid derivative in which anthranilic acid, acting as ammonia or an amine, is substituted in acetic acid.



This compound may be termed **anthranilo acetic acid**, but as it is also a phenyl substituted **glycine** or **amino acetic acid** it is termed **phenyl glycine ortho-carboxylic acid**. The rest of the synthesis of indigo will be discussed under indigo itself, but as it all involves the original synthesis of anthranilic acid from a cheap raw material and as the phenyl glycine *ortho*-carboxylic acid is an amino aromatic acid, this much has been given here.

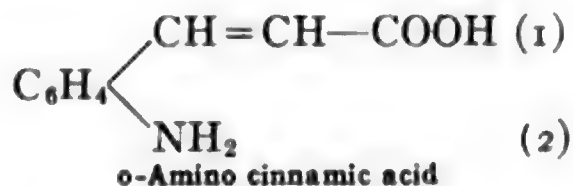
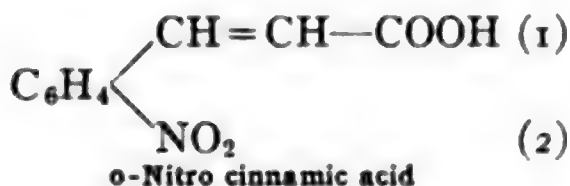
Methyl Anthranilate.—The methyl ester of anthranilic acid, **methyl**

anthranilate, $\text{C}_6\text{H}_4 \begin{cases} \text{COOCH}_3 & (1) \\ \text{NH}_2 & (2) \end{cases}$, is a constituent of the *oil of orange*

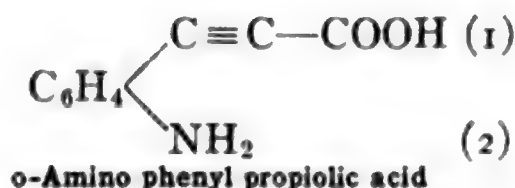
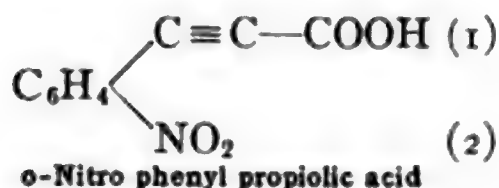
blossoms (*Neroli oil*) or of sweet orange peel and the oil of Jasmin flowers. It is valuable as a perfume.

Nitro and Amino Cinnamic Acids.—Two other nitro aromatic acids and their corresponding amino acids should be mentioned all of which

have been associated with the development of the synthesis of idigo. These are **ortho-nitro cinnamic acid** and **ortho-amino cinnamic acid**, which are side-chain-carboxy acids with an ethylene unsaturated or double bond group.



ortho-Amino Phenyl Propiolic Acid.—The corresponding acetylene unsaturated or triple bond acid is **phenyl propiolic acid**. The nitro and amino derivatives are



The latter pair of acids may be formed from the former by loss of hydrogen bromide from the side-chain bromine substitution product.

Phenyl Alanine.—Phenyl propionic acid yields a side-chain-substituted amino derivative which is **alpha-amino beta-phenyl propionic acid**. As *alpha*-amino propionic acid is known as **alanine** this phenyl derivative is named **phenyl alanine**.



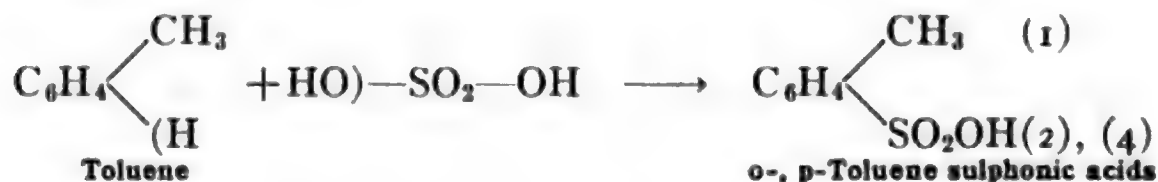
It is obtained as one of the *amino acid cleavage products* of the hydrolysis of proteins (p. 389).

Azo, Hydrazo and Diazo Acids.—From the nitro aromatic acids there may be obtained on proper reduction of the nitro group (p. 537) the corresponding *azo* and *hydrazo* compounds which bear exactly the same relation to the nitro acids and amino acids that the simple **azo** and **hydrazo benzene** do to nitro benzene and aniline. Also from the amino acids by diazotization we may obtain *diazo acids*. These diazo acids may be used as intermediate products in preparing other substituted acids from the amino acids by replacing the diazo group with other groups by any of the diazo reactions (p. 600). Historically the diazo-benzoic acids are important as it was with these compounds that **Griess** first carried out his investigations.

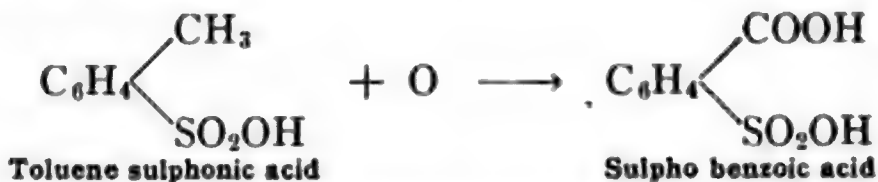
SULPHO AROMATIC ACIDS

The **sulpho aromatic acids** are mixed sulphonic acid and carboxy acid derivatives of the hydrocarbons. They may be prepared by sulphonating the aromatic acid directly in which case the *meta* product is obtained. To prepare the *ortho* or *para* compounds a hydrocarbon is first sulphonated and then the side chain is oxidized to carboxyl.

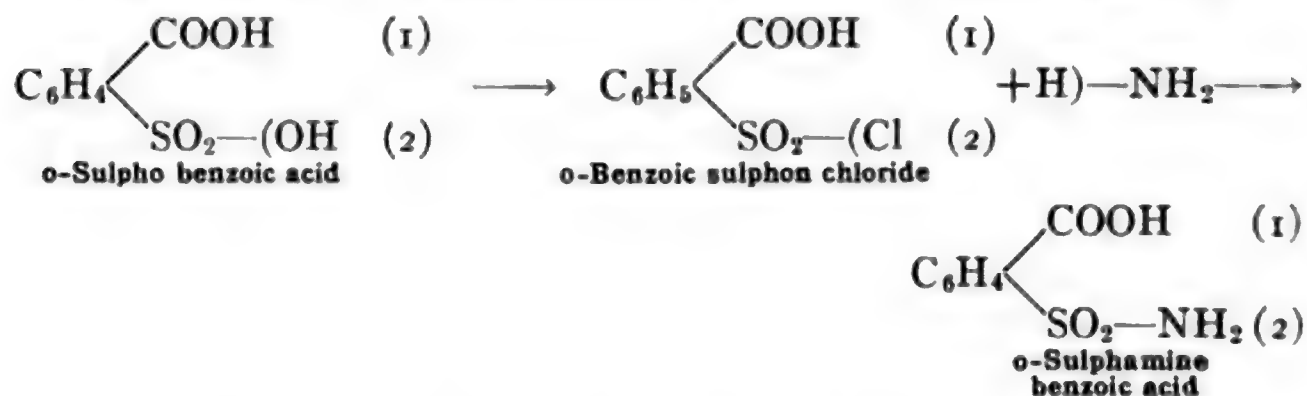
Sulpho Benzoic Acid.—When toluene is sulphonated with concentrated sulphuric acid a mixture of *ortho* and *para* toluene sulphonic acid is obtained.



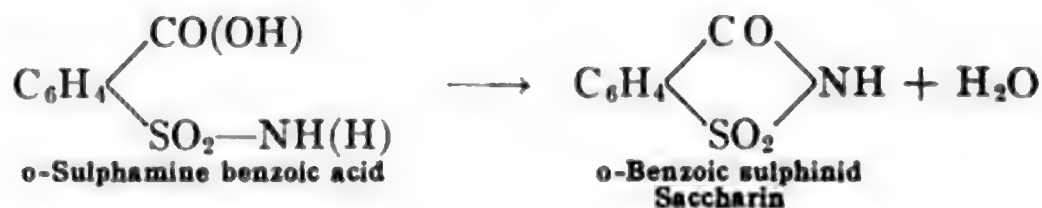
On oxidation of these compounds the products are the corresponding **sulpho benzoic acids**.



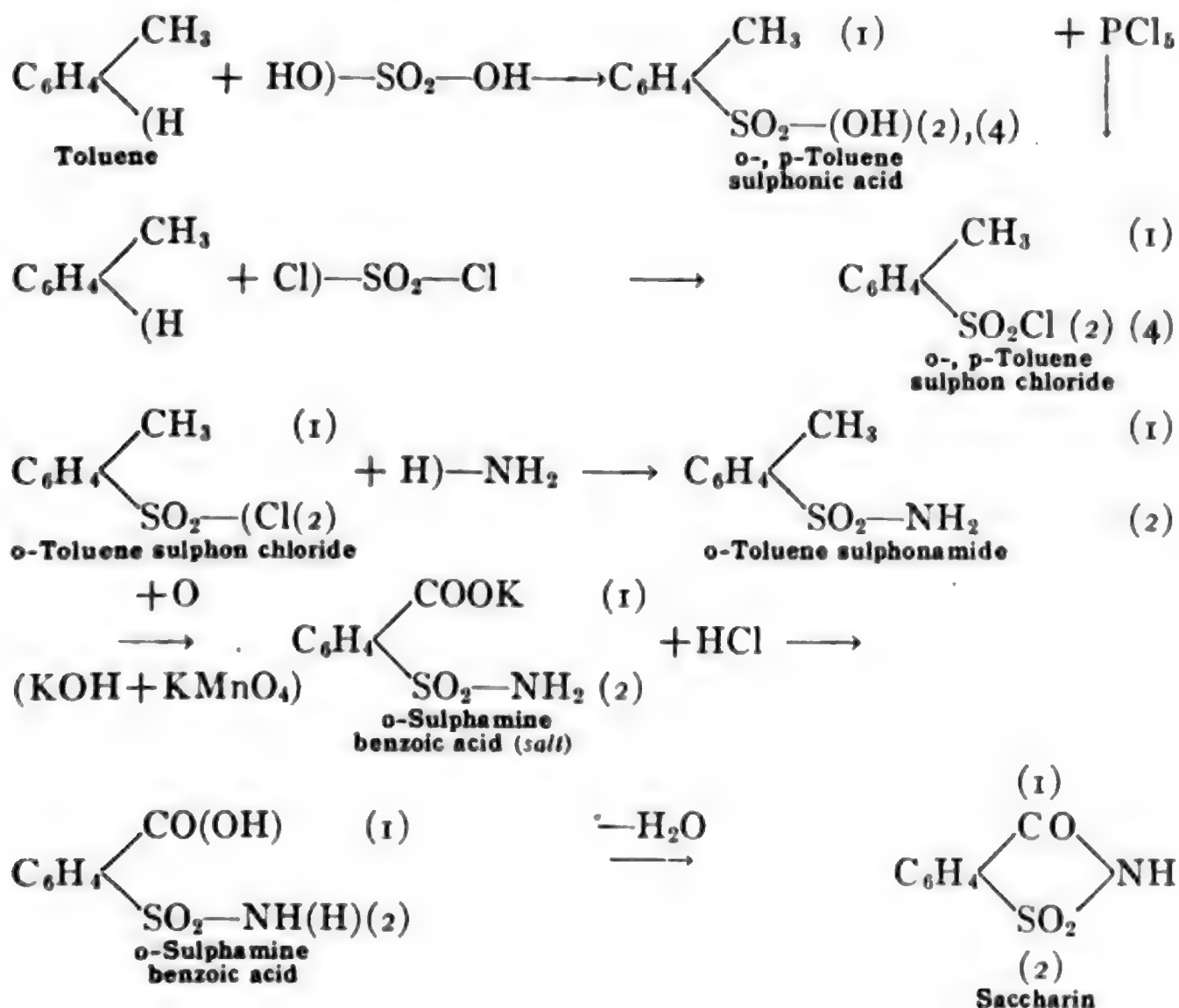
Saccharin.—When *ortho*-sulpho benzoic acid is treated with phosphorus pentachloride the *sulphonic acid* group yields the *sulphon chloride* group and this with ammonia yields the *sulphamine* group.



Now *ortho*-sulphamine benzoic acid readily loses water and yields an *imide anhydride*.



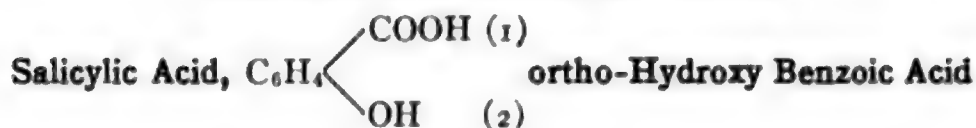
Saccharin Synthesis.—This anhydride, or **ortho-benzoic sulphinid**, is a very sweet non-carbohydrate substance and has been named **saccharin**. It is about three hundred times as sweet as cane sugar. In practice the reaction is carried out a little differently. Toluene is sulphonated and then converted into the corresponding sulphon chlorides which will be a mixture of the *ortho* and *para* compounds. The toluene is still better converted directly into the mixed *ortho* and *para*-toluene sulphon chlorides by treatment with **sulphuryl chloride**, SO_2Cl_2 . The mixed sulphon chlorides are then separated by filtering with ice, the *para* compound being solid while the *ortho* is a thick oily liquid. The pure **ortho-toluene sulphon chloride** is then treated with ammonia and converted into the **ortho-toluene sulphonamide**. The *ortho*-toluene sulphonamide is then oxidized with alkaline potassium permanganate to the potassium salt of **ortho-sulphamine benzoic acid**. On acidifying, *ortho*-sulphamine benzoic acid is obtained which loses water at once and the product is saccharin.



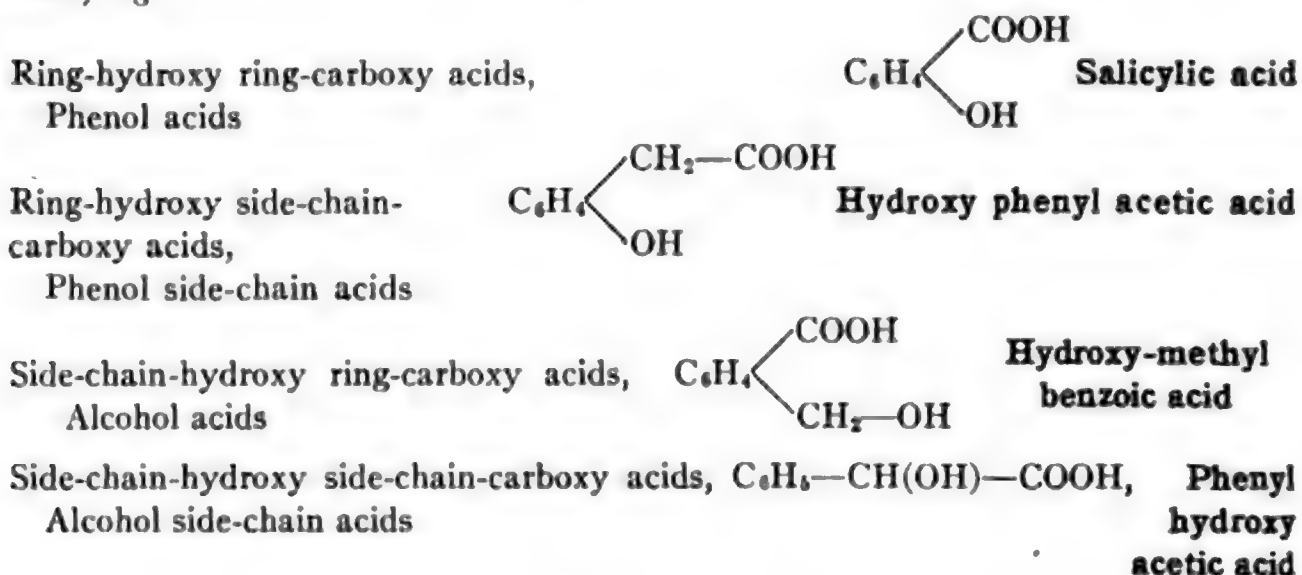
Saccharin was discovered in 1879 by **Remsen** and **Fahlberg**. It is only slightly soluble in cold water, but is soluble in hot water, acetone, alcohol or ether. From acetone it crystallizes in beautiful crystals. It is a valuable medicinal substance as it can be used for its sweetening effect in food, by persons who have the disease known as *diabetes* and who are unable to use cane sugar, and only a minimum of any carbohydrate food. It does not possess any nutritive value, however. It is also used as a food preservative, but its use is restricted or prohibited by most pure food laws. It is interesting that only the *ortho*-sulphamine benzoic acid yields such a sulphinid anhydride. The *para* compound, on heating, yields other products.

HYDROXY AROMATIC ACIDS

PHENOL RING-CARBOXY ACIDS



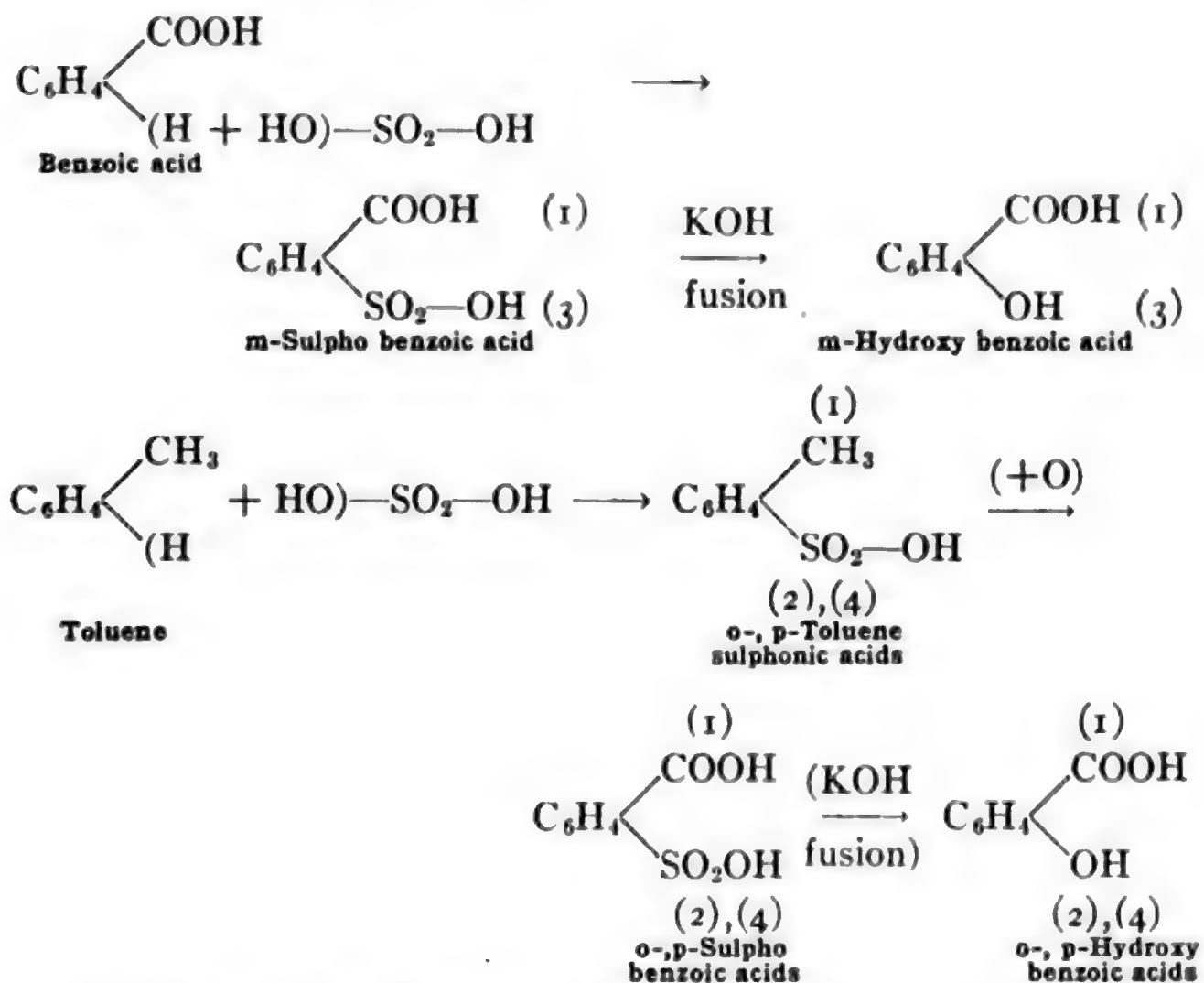
The hydroxy aromatic acids constitute an important group. They may be of the several types given in the introductory general discussion, *e.g.*



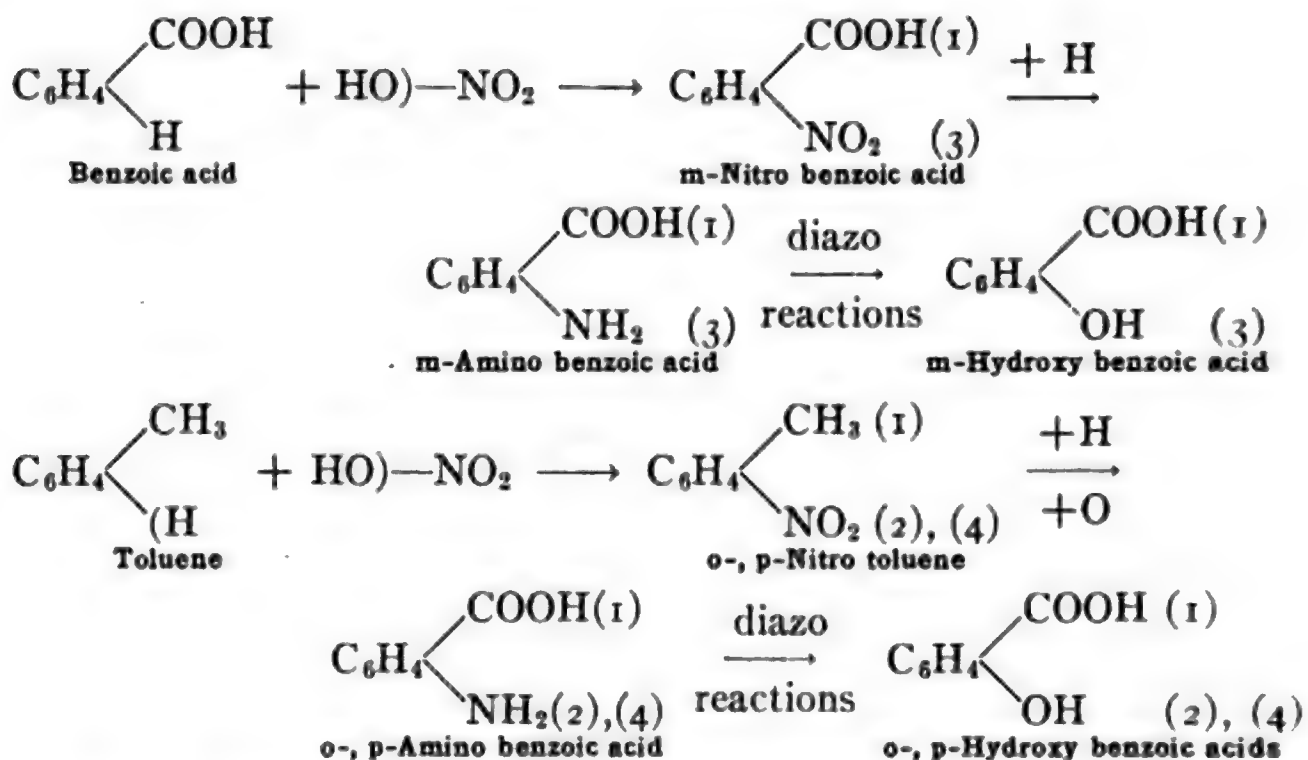
The most important of the *ring-hydroxy acids* or *phenol acids*, is the **ortho-hydroxy benzoic acid** commonly known as **salicylic acid**, with the formula given above. We may use this and the isomeric hydroxy benzoic acids (*meta* and *para*) as our illustration for the general methods of preparing phenol acids. As these compounds are mixed *phenols* and aromatic ring-carboxy *acids* two general methods are possible for their synthesis. (1) General methods for preparing phenols, in which

case we start with ring-substituted ring-carboxy acids. (2) General methods of preparing acids, in which case our starting point will be substituted phenols or phenols of benzene homologues.

From Sulpho Benzoic Acid.—The most common method of preparing phenols is by the *alkali fusion* of the *sulphonic acids*. Sulpho benzoic acids will thus yield hydroxy benzoic acids. In case the sulpho benzoic acid has been made by direct sulphonation of benzoic acid the *meta* compound will result. If, however, we start with *toluene* and sulphonate it we will obtain the *ortho* and *para* compounds.



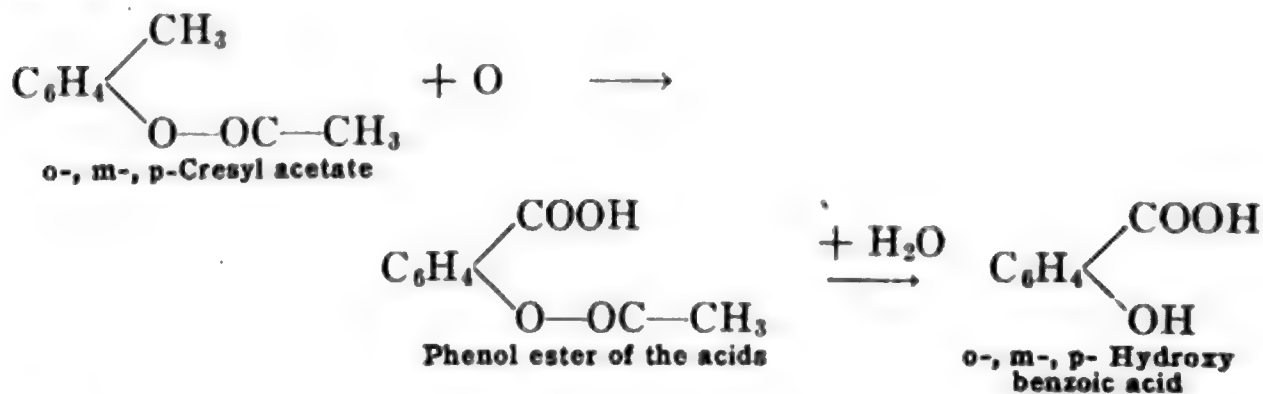
From Amino Benzoic Acid.—Amino acids by the diazo reaction and decomposition with water will yield the corresponding phenol acids. In such cases also if we start with benzoic acid, nitrate directly and reduce this to the amino compound, the final product of the diazo reaction will be the *meta* hydroxy acid. If we start with *toluene* and nitrate it and then proceed as in the foregoing and oxidize the amino toluene to amino benzoic acid our product will be the *ortho* and *para* hydroxy acids.



From Phenol.—General methods for preparing acids may be applied first to the phenols of benzene homologues. Thus by the oxida-

tion of the three cresols, hydroxy toluenes, $\text{C}_6\text{H}_4 \begin{array}{l} \text{CH}_3 \\ \text{OH} \end{array}$, we should

obtain the corresponding hydroxy acids. An interesting fact, however, is that the presence of the hydroxyl group in the ring protects the methyl group from oxidation and we cannot thus oxidize the cresols as indicated. If we convert the phenol into a phenol ether or a phenol ester, however, the oxidation will take place, the ester being then hydrolyzed to the acid.



This method is not often used.

Kolbe Synthesis from Phenol by Carbon Dioxide.—The most important method of synthesizing the phenol acids from the phenols is by an interesting reaction known as the **Kolbe synthesis**, and especially

applicable to **salicylic acid**. It consists in the direct introduction of **carbon dioxide** into the benzene ring of a phenol thus producing a carboxyl group. We have shown that formic acid is the reduction product of carbon dioxide (p. 135).



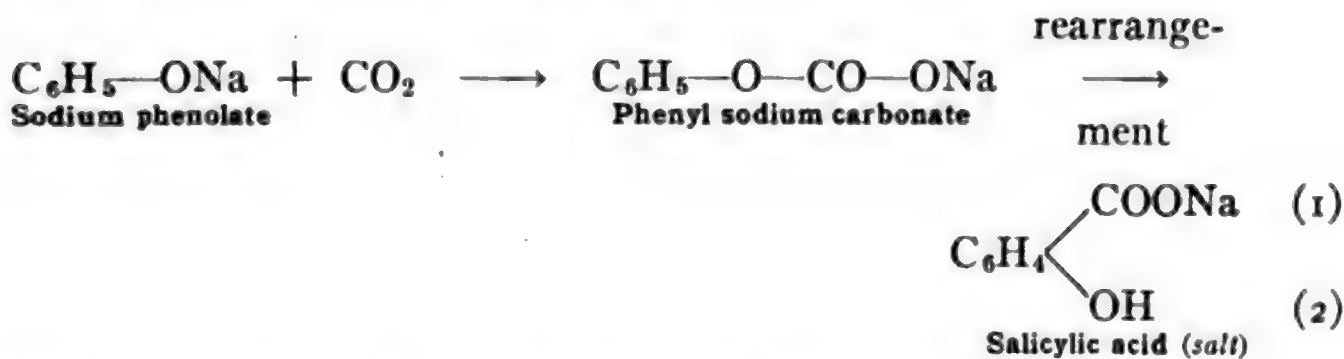
Metallic alkyls yield aliphatic acids with carbon dioxide.



Also mono-brom benzene and sodium yield benzoic acid with carbon dioxide.

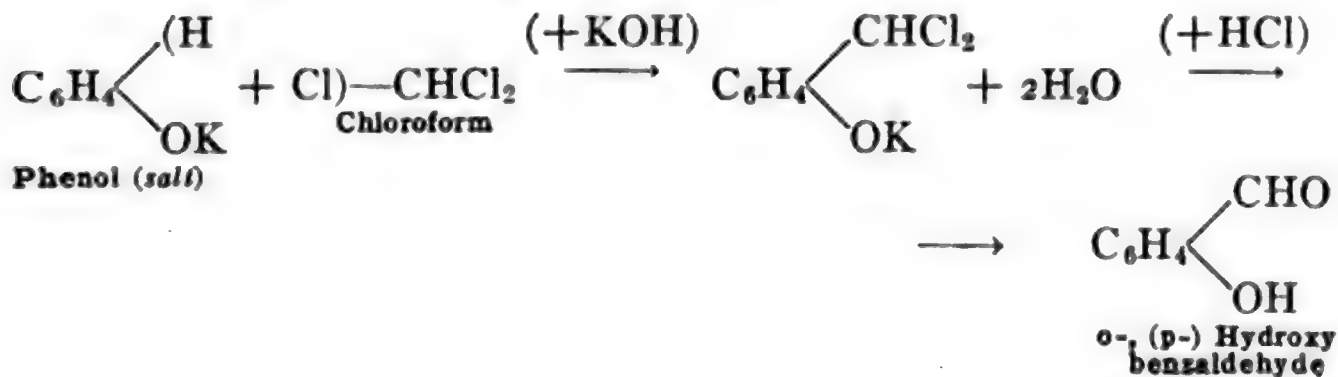


In all of these cases the carboxyl group results from the direct introduction of carbon dioxide in front of a hydrogen or sodium atom. Now the sodium compound of phenol, viz., **sodium phenolate**, $\text{C}_6\text{H}_5\text{—ONa}$, undergoes a similar reaction yielding first a phenyl ester of carbonic acid which rearranges into **salicylic acid**.

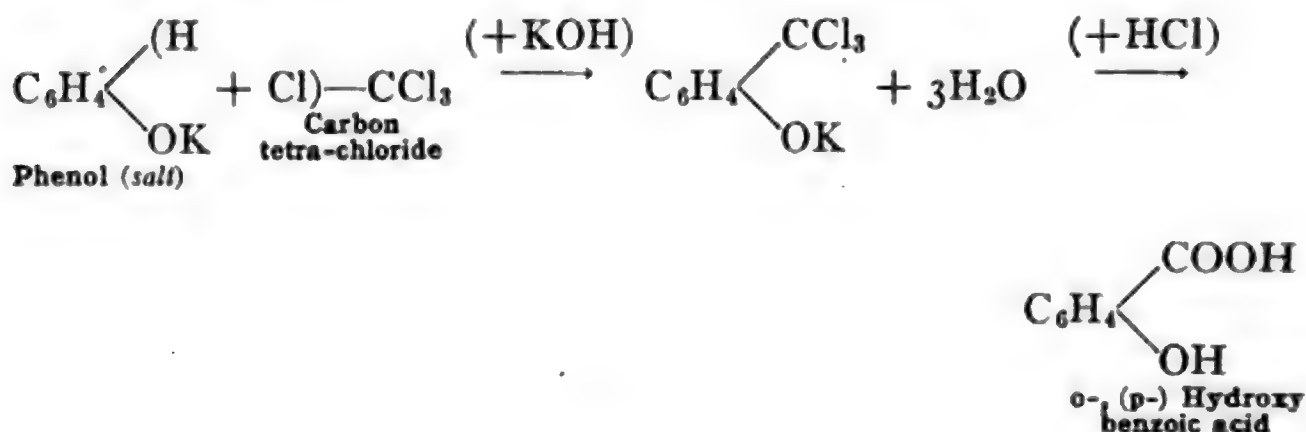


The *meta* and *para* hydroxy acids are not formed by this reaction but if potassium is used in place of sodium the product is largely the *para*-hydroxy acid.

From Phenols by CCl_4 .—The **Reimer-Tiemann** reaction for the synthesis of hydroxy aldehydes (p. 659) is:



The principle of this reaction allows the synthesis of hydroxy acids if instead of chloroform we use carbon tetra-chloride, CCl_4 .

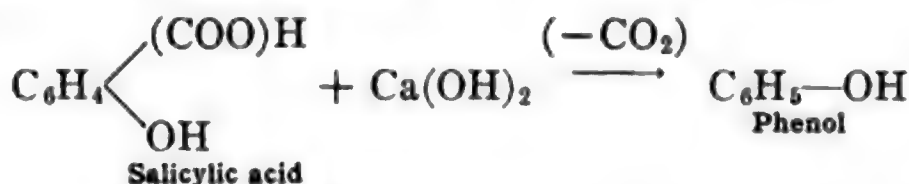


From Phenol Alcohols and Phenol Aldehydes.—The phenol alcohols and phenol aldehydes will of course yield phenol acids on oxidation. Reactions for these need not be written as they have been given in general at various times. **Salicylic acid** or **ortho-hydroxy benzoic acid** has the constitution assigned to it as proven by the syntheses just discussed.

Salicin.—It derives its name from the glucoside **salicin** which is present in the bark of willow trees, the generic name of which is *Salix*. When the glucoside is hydrolyzed it yields **glucose** and a compound known as **saligenin**, which is **salicylic alcohol** or **ortho-hydroxy benzyl alcohol**, and which on oxidation yields salicylic acid. This is one of the natural sources of the acid.

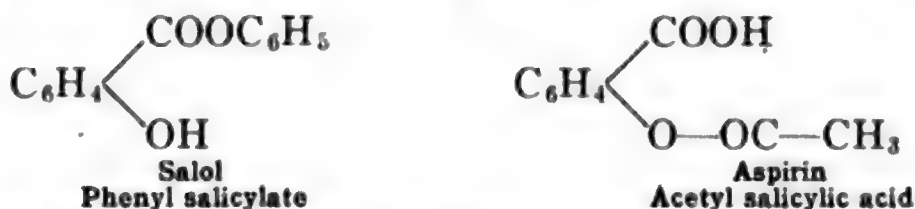
Oil of Wintergreen. Methyl Salicylate.—The most interesting natural source of the acid, however, is *oil of wintergreen* obtained from the wintergreen plant, *Gaultheria procumbens*. The chief constituent of this oil is the *methyl ester* of salicylic acid, **methyl salicylate**, $\text{C}_6\text{H}_4 \begin{array}{l} \text{COOCH}_3 \text{ (1)} \\ \text{OH (2)} \end{array}$. On boiling the oil with dilute acids the salicylic acid is obtained. Synthetic oil of wintergreen is made by esterifying salicylic acid with methyl alcohol. Salicylic acid is a white crystalline solid, m.p. 156° , which sublimes on heating to 200° . It is slightly soluble in cold water, 1 part in 444 parts, but easily soluble in hot water, crystallizing on cooling in fine needles. It gives a violet color reaction with **ferric chloride** in both water and alcoholic solutions by which means it may be distinguished from **phenol** which gives the color reaction in water solutions only. With bromine it is precipitated as a bromine compound,

$C_6H_3Br_2-OBrl$. When heated alone, but better with lime, it loses carbon dioxide and yields phenol.

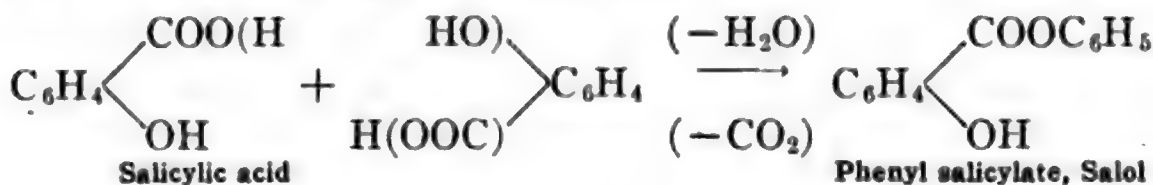


Medicinal Properties.—Salicylic acid is an *antiseptic* and *preservative*, being used in the preservation of foods, though generally restricted or prohibited by pure food laws.

Salol and Aspirin.—The sodium salt and several derivatives possess medicinal properties as *internal antiseptics*, as *antipyretics* or temperature reducers, and to lessen the pain of rheumatism. The most common of these are **salol**, which is the *phenyl ester* of salicylic acid, as an acid, and **aspirin**, which is the **acetic acid ester** of salicylic acid, as a phenol.



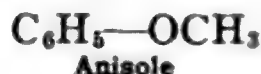
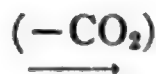
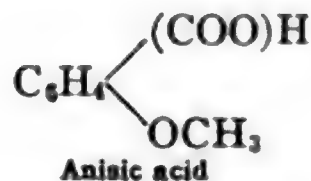
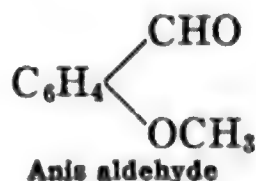
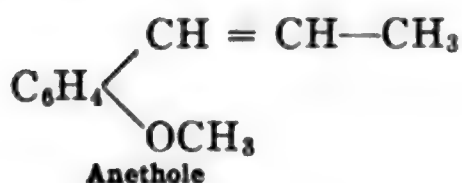
Salol is used as an intestinal antiseptic. It is prepared by heating salicylic acid alone to 160° to 240° . In this case one molecule loses carbon dioxide yielding phenol which then esterifies with another molecule of the acid yielding the phenyl ester.



The reaction is accomplished better by heating to 120° , two molecules of salicylic acid, two molecules of phenol (or sodium phenolate) and one molecule of phosphorus oxychloride, POCl_3 , the reaction here being the same as the second step in the preceding one. **Aspirin** is prepared by acetylating salicylic acid with acetyl chloride in the presence of acetic anhydride, sulphuric acid, zinc chloride or sodium acetate. It also is an antipyretic and antiseptic. Other similar derivatives, *e.g.* **betol**, containing naphthol and quinoline groups, are also medicinal compounds of importance. The medicinal action of these salicylic esters is, that in the intestine they become hydrolyzed and yield salicylic acid or sodium salicylate, which then acts as an antiseptic and antipyretic. The action of these esters is less violent than that of

sodium salicylate itself when taken internally because with them the salicylic acid is liberated slowly.

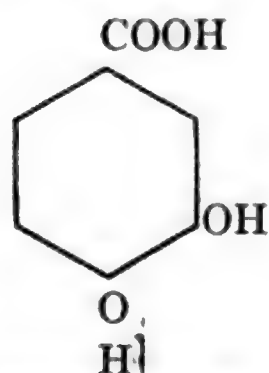
Anisic Acid.—A derivative of **para-hydroxy benzoic acid** is the methyl ether, $\text{C}_6\text{H}_4 \begin{matrix} \text{COOH (1)} \\ \text{OCH}_3 \text{ (4)} \end{matrix}$, known as **anisic acid**. It is related to **anethole** and **anis aldehyde** (p. 661), and like them occurs in *oil of anis seed*. On heating it loses carbon dioxide and yields **anisole**, **methyl phenyl ether**.



POLY-HYDROXY MONO-RING-CARBOXY ACIDS

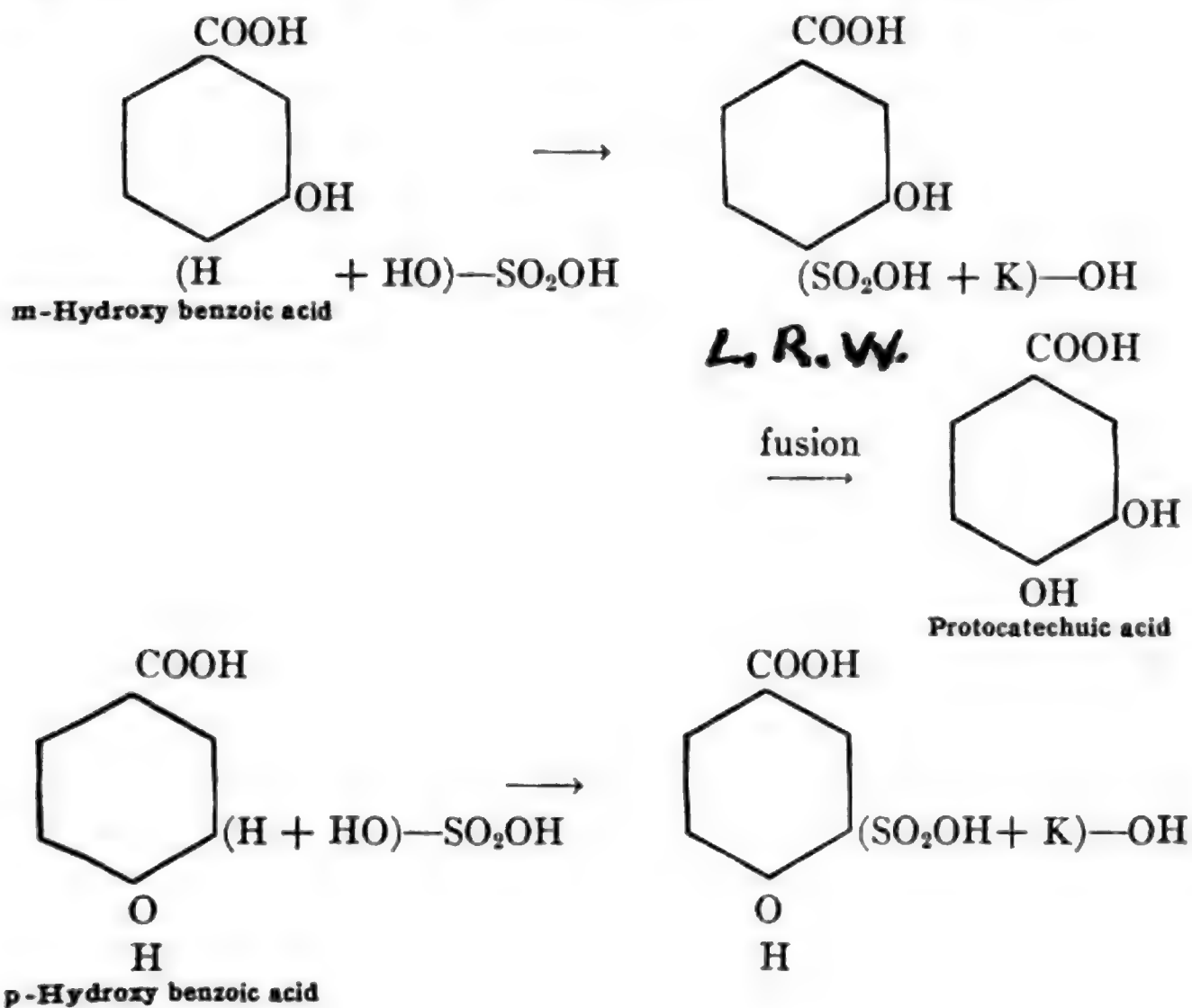
When more than one hydroxyl group is substituted in the ring of an aromatic acid there will result *poly-phenol acids*, *i.e.*, *poly-hydroxy acids*. The poly-hydroxy benzoic acids, which include the most important members, bear the same relation to benzoic acid that the ordinary poly-phenols, *e.g.*, **pyrocatechinol**, **resorcinol**, **pyrogallol**, etc. (p. 617), do to benzene. They may also be considered as carboxyl substitution products of the poly-phenols.

Protocatechuic Acid.—One of the di-hydroxy benzoic acids is related to vanillin, which we have already studied. The acid is known as **protocatechuic acid**, and derives its name from the fact that it may be obtained from a gum or resin, known as *gum catechin*, by fusion with potash, *i.e.* by heat and oxidation in presence of an alkali. A large variety of plant products including *alkaloids*, *essential oils*, *gums*, *resins* and *tannins* yield this acid. The following may be mentioned: *gum catechin*, *gum benzoin*, *guaiac resin*, *myrrh*, *piperine* or *piperic acid*, *vanillin*, *caffe-tannic acid*. These natural sources at once suggest a relationship to vanillin (p. 661) and heliotropin (p. 662). It is the acid corresponding to **protocatechuic aldehyde**, **3-4-di-hydroxy benzaldehyde** (p. 661), which explains the relationship just mentioned. Its constitution, is then:

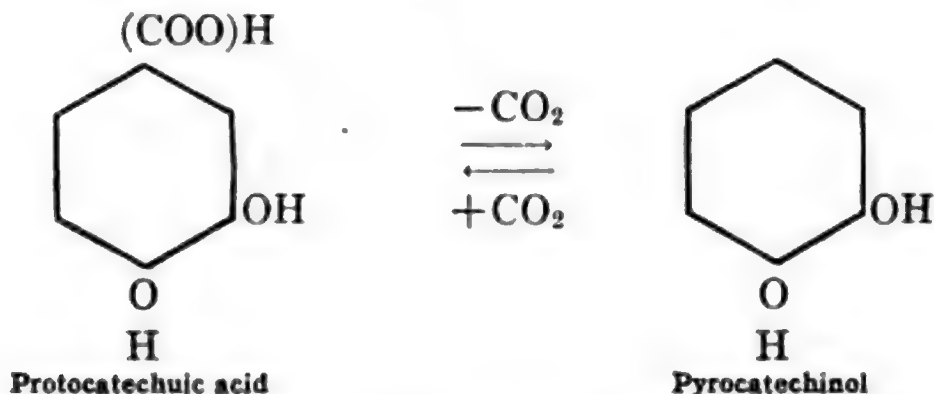


Protocatechuic acid
1-Carboxy 3-4-dihydroxy benzene

Synthesis from meta- or para-Hydroxy Benzoic Acid.—The constitution is proven by its synthesis by *sulphonation* and then *alkali fusion* of either **meta-hydroxy benzoic acid** or **para-hydroxy benzoic acid**. As this synthesis introduces into each of these acids first a sulphonic acid group and then in place of this a second hydroxyl group the two hydroxyls in the final product, protocatechuic acid, must be in the 3-4 positions as only such positions could be occupied in a product obtained from either the *meta* or *para* hydroxy benzoic acid.

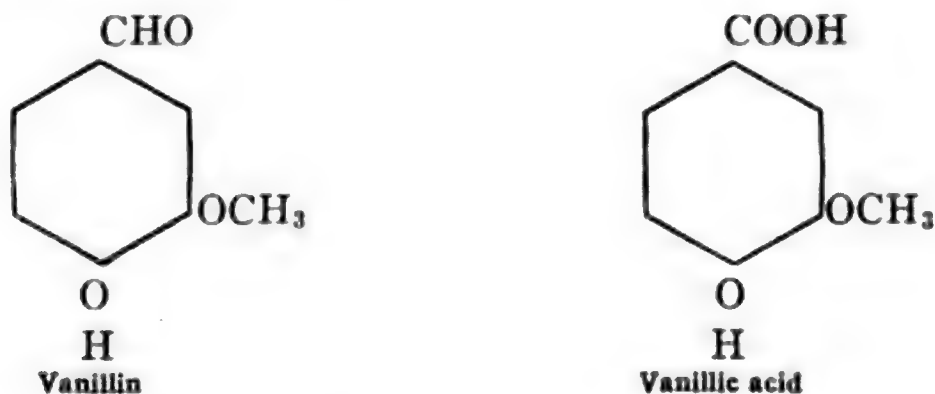


This proof is exactly analogous to that for the constitution of **pseudocumene**, **1-3-4-tri-methyl benzene** from either **meta-xylene** or **para-xylene** (p. 490). That the two hydroxyls are ortho to each other is proven by the fact that on heating with lime protocatechuic acid yields **pyrocatechinol**, **1-2-di-hydroxy benzene**.



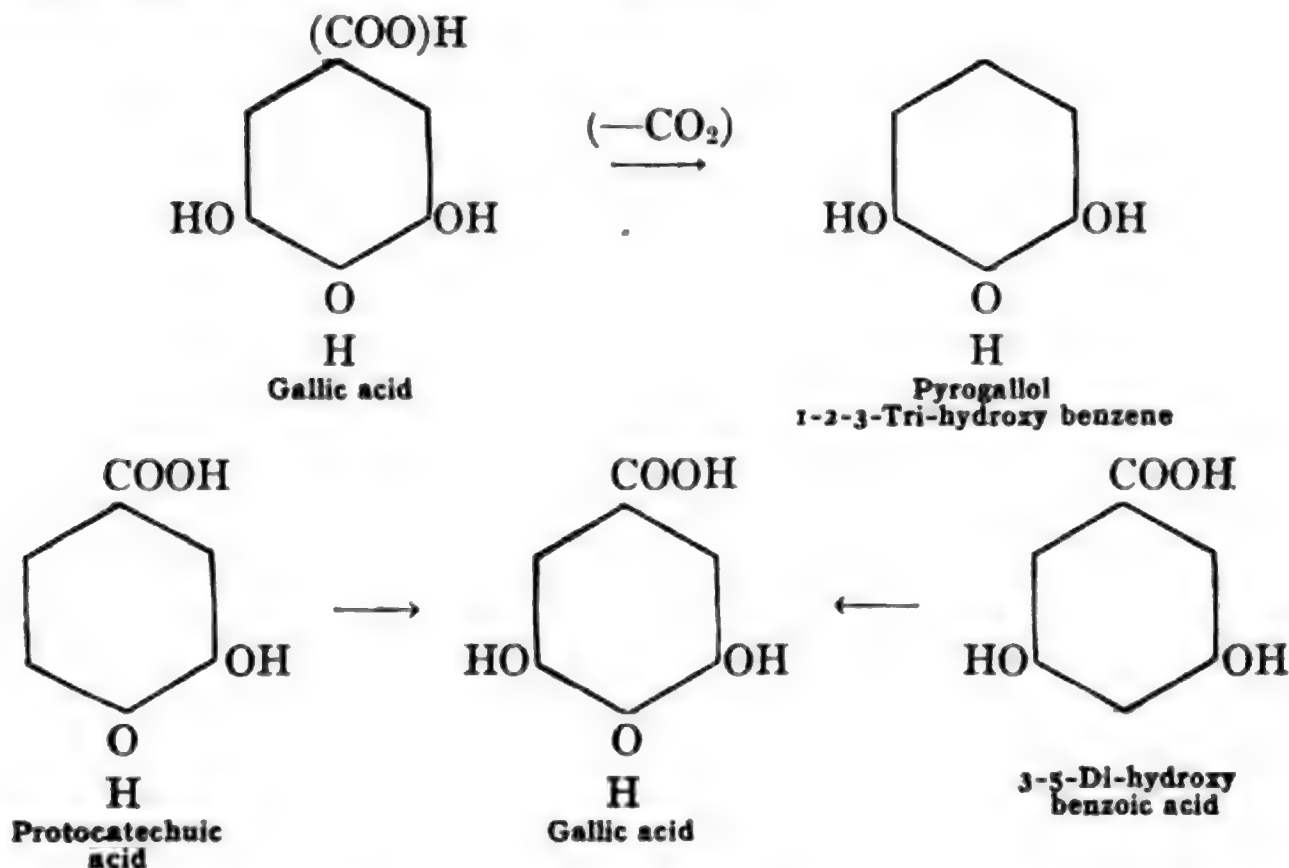
This relationship explains the similarity of the names and the fact that both are obtained from *gum catechin*. The reverse of the above reaction, the synthesis of protocatechuic acid from pyrocatechinol, may be accomplished by heating the phenol with ammonium carbonate and water to 1400° under pressure, which is a modification of the **Kolbe** reaction for synthesizing salicylic acid (p. 716). From its constitution and by reference to the formulas on page 662 we will see its relationship to **vanillin**, **heliotropin**, **eugenole**, **safrole**, **guaiacol**, etc.

Vanillic Acid.—The *mono-methyl ether* with the *methoxy* group in the *3-position* is known as **vanillic acid**, as it is the acid corresponding to the aldehyde **vanillin**.



Gallic Acid.—The **3-4-5-tri-hydroxy benzoic acid** is known as **gallic acid**. The proofs of this constitution are (1) that on heating with lime and the loss of carbon dioxide we obtain **pyrogallol** which has been proven to have the constitution **1-2-3-tri-hydroxy benzene** (p. 619); and (2) that it may be synthesized from either **brom-protocate-**

chuic acid in which the two hydroxyls are in the 3-4-positions or from brom **3-5-di-hydroxy benzoic acid**. Therefore the three hydroxyls in **gallic acid** must be in the 3-4-5-positions.



Gallic acid is found free or as a glucoside, from which it is set free on hydrolysis, in several plants, *e.g.* *sumach*, *gall nuts*, *acorns*, *Chinese tea*, *Divi-divi*, etc. It is also formed by the acid hydrolysis of tannins which occur in these or similar plants which possess astringent properties. With ferric chloride solution gallic acid throws down a blue-black precipitate which is soluble in excess of the ferric chloride giving a green solution.

Tannic Acids.—Closely related to gallic acid and to protocatechuic acid is a group of acids known as **tannic acids**. While the exact constitution of these is not known it is probable that they are *anhydrides* of different *hydroxy benzoic acids*, similar to the *di-saccharoses* as anhydrides of *mono-saccharoses*. This is indicated by the fact that on hydrolysis the tannic acids yield hydroxy benzoic acids. The different tannic acids are given names that indicate the hydrolytic products or the natural source.

Gallo-tannic Acid.—One of these is **gallo-tannic acid**, also known as simply **tannic acid**, or **tannin**, also as **di-gallic acid**. It is found in *gall-nuts* and in *tea* and yields gallic acid on hydrolysis.



Catechu-tannic Acid.—A tannic acid which is found in *gum catechin* and which yields **catechin**, **protocatechuic acid** and **pyrocatechinol** is known as **catechu-tannic acid**.

Querci-tannic Acid.—Another tannic acid, probably also a catechu-tannic acid, as it yields the same products as above, is known as **querci-tannic acid**. It derives this name from *Quercus*, the generic name for the oak tree, as it is found in oak bark, but not, however, in *oak galls*.

Caffe-tannic Acid.—Another tannic acid is found in *coffee berries* and, therefore, is called **caffe-tannic acid**. It differs from the other tannic acids in not precipitating gelatin and can not be used in tanning hides. It is possibly simply a coloring substance like the yellow coloring matter of *gum fustic*, *fustian yellow* or **maclurin**. It is sometimes termed a **pseudo-tannin**.

Tannins.—It has just been stated that the tannic acids are probably *anhydrides* of *poly-hydroxy benzoic acids*, especially **protocatechuic acid** and **gallic acid**. Also while gallic acid is found free in gall-nuts and certain astringent plants it is probably formed by the hydrolysis of *glucosides* in the plant. The glucoside mother substances of the tannic acids are known as **tannins**. Recent work of **Fischer** has shown that tannin is undoubtedly a glucoside of five molecules of **di-gallic acid** or **gallotannic acid**, and one molecule of **glucose**. The term **tannin**, while ordinarily used as synonymous with **tannic acid**, is more correctly a class name for a group of astringent plant products which possess certain general characters. Some of the characteristics of tannins are as follows: (1) They are astringent colloidal substances. (2) They precipitate gelatin and form insoluble products with gelatin-yielding substances such as animal skins. This is the property which makes them useful in tanning hides into leather. This property is not possessed by **caffe-tannic acid**, which is the reason for considering it more truly a coloring matter or a pseudo-tannin. (3) With ferric chloride they produce a blue-black or a green color. This property is utilized in the manufacture of iron inks.

Tannins occur quite widely distributed in the plant kingdom giving to the plant characteristic astringent properties. The most common

sources of tannins are the *gall-nuts* formed by insects on various plants such as oak, tamarix, etc.; the bark and wood of *oak*, *chestnut*, *pine*, *acacia*, *hemlock*, *eucalyptus*, etc.; the leaves of *sumach* and the roots of *canaigre*. The different tannins have been classified by **Procter** into two divisions similar to those given for the classification of the tannic acids.

1. *Pyrogallic acid tannins* which yield tannic acids convertible into **gallic** and **pyrogallic acids**. These tannins give a blue-black color with ferric chloride and give no precipitate with bromine water. They also form a bloom on the leather from hides which have been treated with them. These include tannins of *gall-nuts*, *sumach*, *oak* and *chestnut* wood.

2. *Pyrocatechinol tannins* which yield tannic acids convertible into **protocatechuic acid** and **pyrocatechinol**. These tannins give a green-black color with ferric chloride and yield a precipitate with bromine water. They do not produce a bloom on leather in tanning, but yield a red color to it. These include tannins of *oak bark*, *pine bark*, *acacia*, *canaigre*, etc.

Tanning.—The chief use of the tannins is in the process known as tanning. Due to the property of precipitating gelatin they form an insoluble material in the pores of gelatin-yielding substances, such as animal skins, and thereby convert the skin into a product known as leather. This property, it will be recalled, is not possessed by the tannic acid found in coffee beans. The use of tannins for the process of tanning is not so universal as formerly owing to the discovery that similar results can be obtained by the use of **chromic acid**. Leathers produced by tanning with chromic acid are usually cheaper and do not seem to be so impervious to water, though the wearing quality seems to be as good as that produced by oak bark tannin. Tannins are also used as mordants in dyeing.

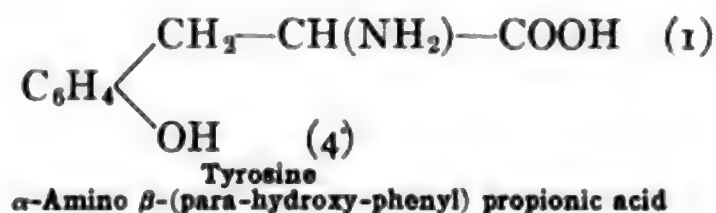
Inks.—Formerly all writing inks except so-called *India ink*, which is a carbon product, were made by the treatment of ferric salts with tannin or tannic acid. The green solution produced with excess of the iron salt becomes black on drying and exposure to the air. Such iron inks may be bleached by means of **oxalic acid** which reduces the colored ferric compound, produced with the gallotannic acid, to a colorless compound. At the present time many writing inks are made from *aniline dyes*. These are not bleached with oxalic acid, but are

completely decolorized by **chlorine** or by *Javelle water*, which is a solution of **sodium hypochlorite** made from *bleaching powder*, crude **calcium hypochlorite**, by precipitating the calcium with sodium carbonate and filtering.

PHENOL SIDE-CHAIN CARBOXY ACIDS

The side-chain carboxy acids which we have studied are **phenyl acetic**, **phenyl propionic** or **hydrocinnamic**, **phenyl acrylic** or **cinnamic** and **phenyl propiolic**. Phenol derivatives of all of these are known. **Hydroxy phenyl acetic acid** is not important.

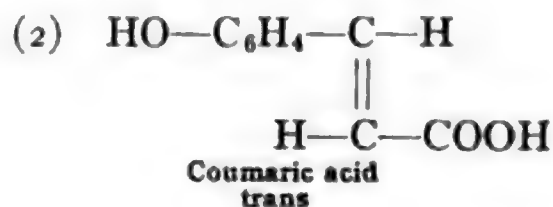
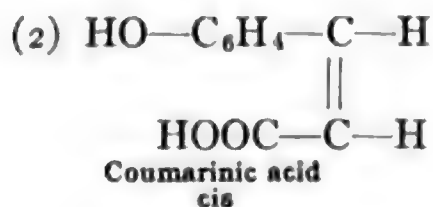
Tyrosine.—**para-Hydroxy-phenyl propionic acid** has a side-chain amino derivative which is one of the amino acid cleavage products obtained by hydrolyzing proteins. It is known as **tyrosine**.



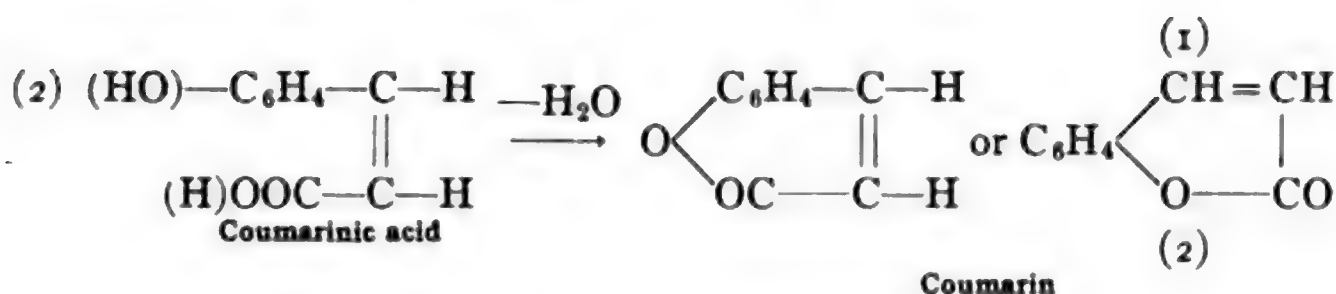
This compound has been discussed in connection with the aliphatic amino acids (p. 389), as its relation to these simpler compounds and to proteins is more important than its relation to the hydroxy aromatic acids.

Hydroxy Cinnamic Acid.—**Cinnamic acid** or **phenyl acrylic acid** yields ring hydroxy derivatives of which the *ortho* compound is the important one.

Coumaric and Coumarinic Acids.—Like cinnamic acid it exists in geometric stereo-isomeric forms, the *trans* form being known as **coumaric acid** and the *cis* form as **coumarinic acid**.

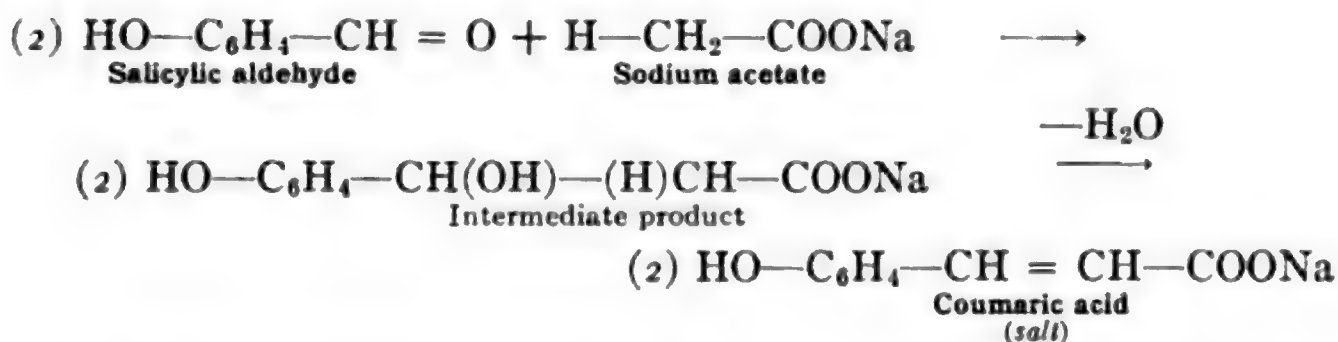


These acids are readily transformed into each other. As in the case of **maleic acid** and **fumaric acid**, the *cis* form easily yields an anhydride while the *trans* form does not. In fact **coumarinic acid**, the *cis* compound, is known only as the anhydride, called **coumarin**.

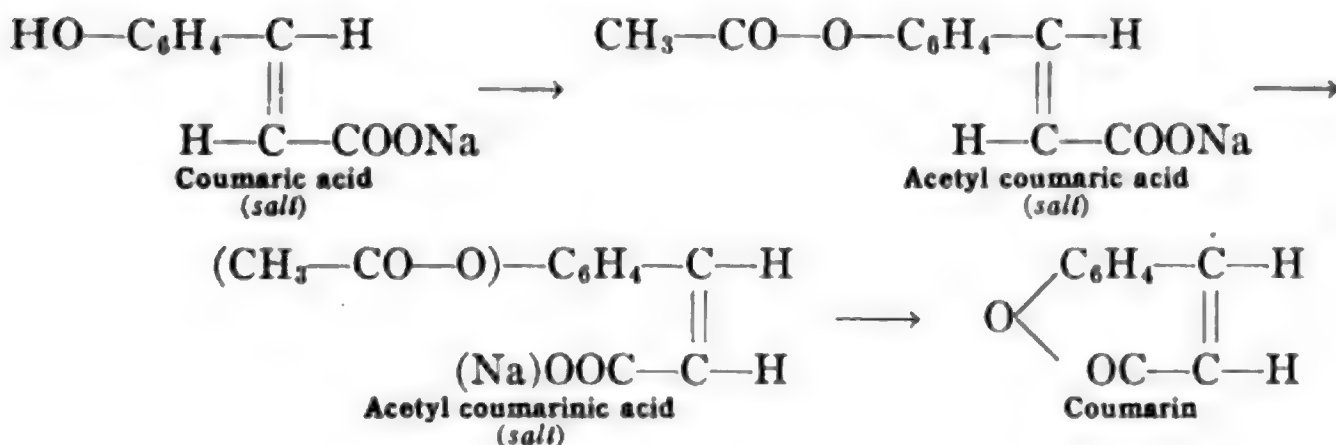


Coumarin. *New-mown Hay.*—**Coumarin** is a pleasant smelling compound, and is the odoriferous constituent of the plant *Asperula odorata* or wood ruff, and also of *new-mown hay*. It is also present in *Tonka beans* the extract of which is used as a substitute for vanilla.

Perkin Synthesis of Coumarin.—**Coumaric acid** and **coumarin** may be synthesized by the **Perkin reaction** for synthesizing unsaturated aromatic acids (p. 698). These syntheses are of historical interest as the two compounds obtained were the first ones prepared by this reaction. Instead of taking a simple aromatic aldehyde it is only necessary to take a *phenol aldehyde*, viz., **salicylic aldehyde**,



The **salicylic aldehyde** is heated with sodium acetate and acetic anhydride when the above reaction takes place. The **coumaric acid** obtained as the sodium salt is then converted into its acetyl derivative. This goes over to the isomeric *cis* form and by the loss of sodium acetate yields the anhydride **coumarin**.



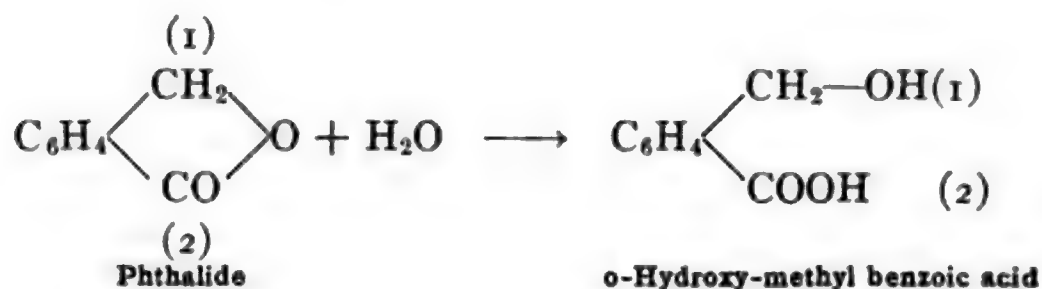
If we examine model formulas of **coumarinic acid** and **coumarin** we will see that the former is really a *delta-hydroxy acid* and the latter, therefore, is a *delta lactone* (p. 243).

ALCOHOL ACIDS

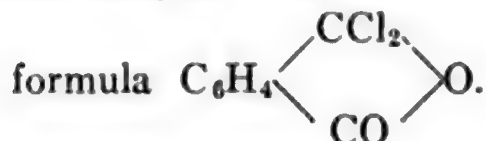
The hydroxy aromatic acids in which the hydroxyl is in the side-chain are alcohol-acid compounds. They therefore possess characters of both alcohols and acids. They may also be of the two types with

the carboxyl in the ring, *e.g.*, $\text{C}_6\text{H}_4 \begin{matrix} \text{CH}_2\text{OH} \\ \text{COOH} \end{matrix}$, **hydroxy-methyl benzoic acid**, or with the carboxyl in the side-chain, *e.g.*, $\text{C}_6\text{H}_5\text{—CH(OH)—COOH}$, **phenyl glycolic acid**. The former type will be prepared by methods characteristic of aromatic alcohols and ring carboxy acids, the latter by those for side-chain-acids and alcohols.

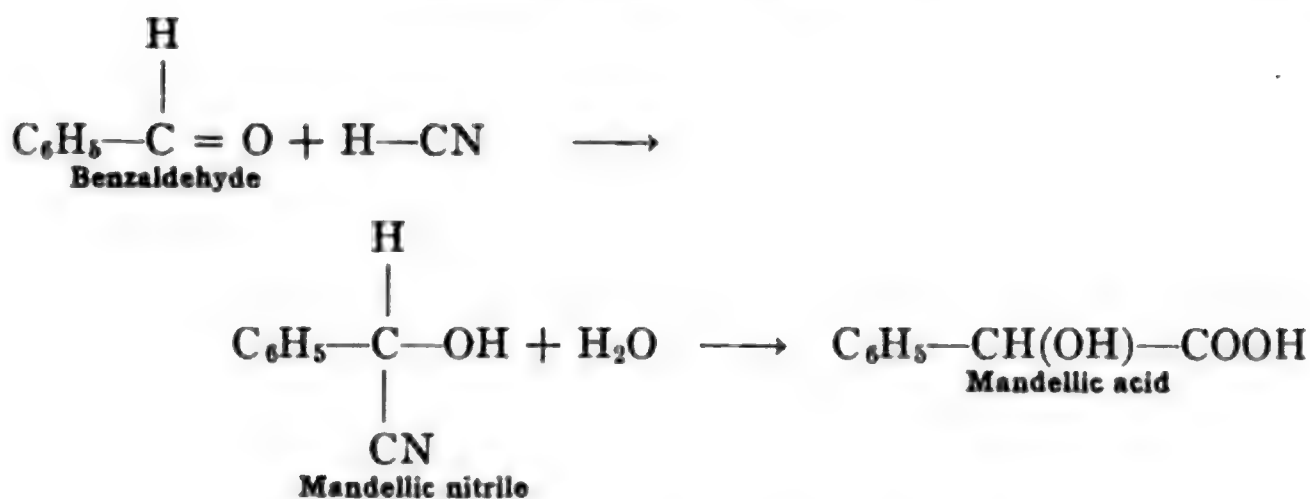
Hydroxy-methyl Benzoic Acid.—The first example given above is important in connection with the constitution of **phthalide** (p. 693) and **phthalyl chloride** (p. 692). By the addition of water phthalide is converted into **o-hydroxy-methyl benzoic acid**.



This reaction establishes the constitution of **phthalide** as a *lactone* not a di-aldehyde and, therefore, phthalyl chloride has the unsymmetrical



Mandellic Acid.—Mandellic acid is **phenyl glycolic acid**, $\text{C}_6\text{H}_5\text{—CH(OH)—COOH}$, **phenyl hydroxy acetic acid**. This constitution is proven by its synthesis from benzaldehyde by condensation with **hydrogen cyanide** and the hydrolysis of the resulting nitrile.



Mandellic acid is the phenyl analogue of lactic acid (p. 246).

$\text{CH}_3-\text{CH}(\text{OH})-\text{COOH}$, **Lactic acid**

$\text{C}_6\text{H}_5-\text{CH}(\text{OH})-\text{COOH}$, **Mandellic acid**

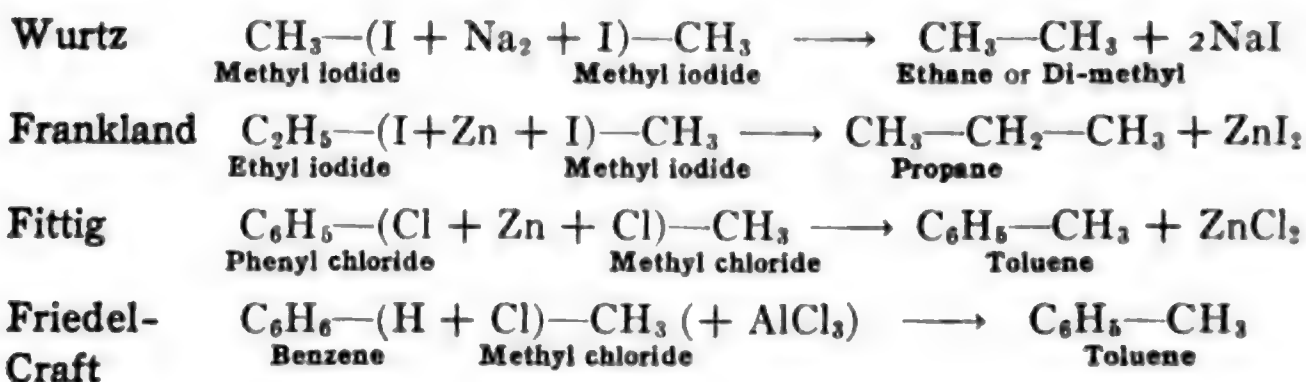
Like lactic acid it contains an *asymmetric carbon* atom and exists as optically active stereo-isomers. The acid synthesized as above is the optically inactive variety while the acid obtained from amygdalin (see below) is *levo* rotatory. The inactive form may be split into its optical components through the cinchonine salts (p. 308). The relationship of the acid to benzaldehyde explains the fact that the two compounds may be obtained from the same glucoside, viz., **amygdalin**. This glucoside, it will be recalled (p. 654), hydrolyzes naturally by means of the enzyme **emulsin**, or by means of acids, into **glucose**, **benzaldehyde** and **hydrogen cyanide**. When amygdalin, therefore, is boiled with hydrochloric acid the synthetic reaction given above takes place and **mandellic acid** is obtained. Amygdalin is present in the oil of bitter almonds the botanical name of which is *Prunus amygdalus*. Mandellic acid gets its name from the German word for almond, viz., *Mandel*.

2. DI-PHENYL AND RELATED COMPOUNDS

Di-phenyl, $C_6H_5-C_6H_5$

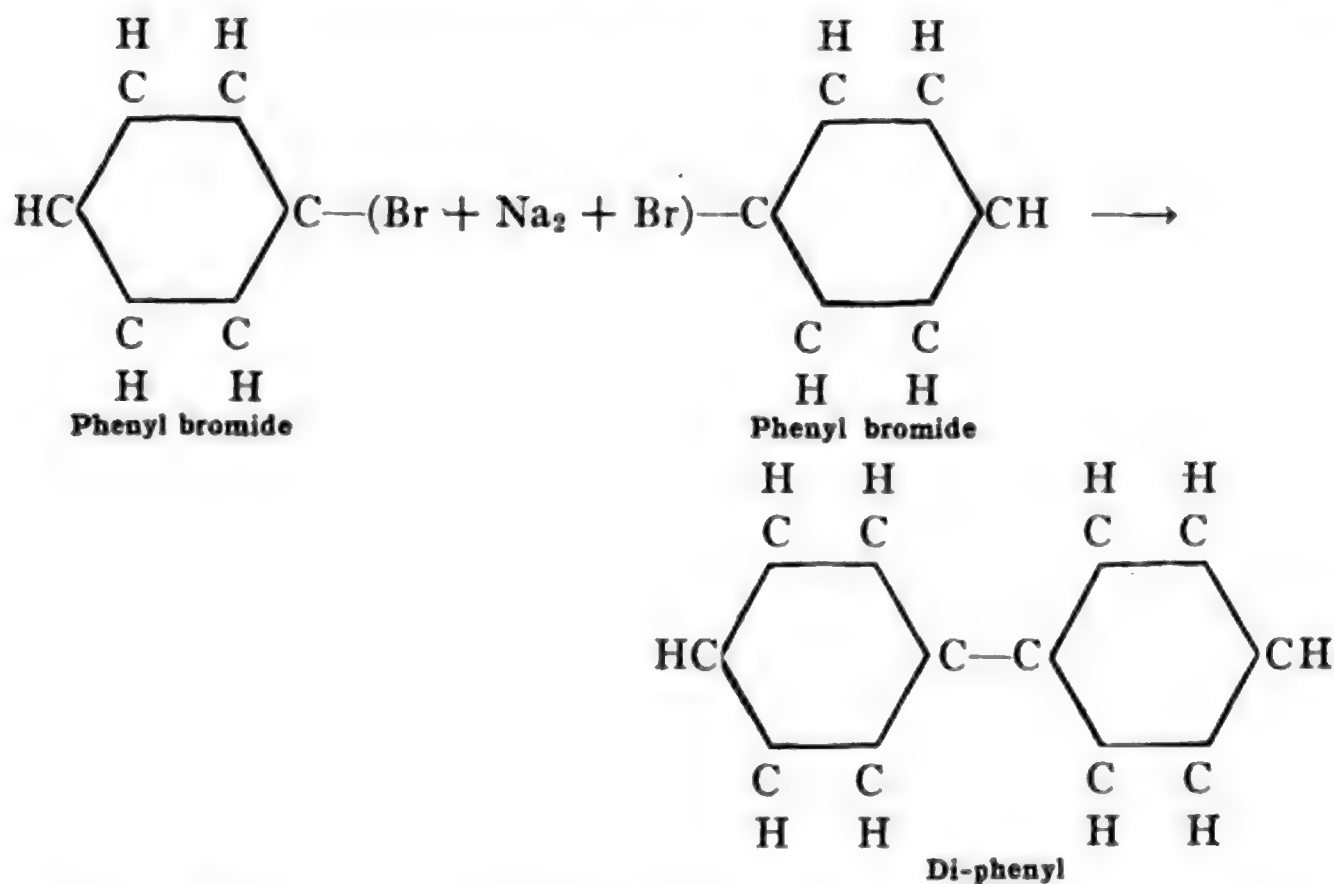
As aromatic compounds we have thus far considered representative members of all of the important classes and sub-classes which have been derived from benzene or its homologues. The homologues include higher hydrocarbons which result from the substitution of one or more aliphatic radicals, either saturated or unsaturated, into a single benzene ring. Thus in the hydrocarbons of the benzene series proper there is only one benzene ring. There are other hydrocarbons, however, which are related to benzene but which are not simple homologues as above defined. They belong to a new and distinctly different series. The characteristic of the series of hydrocarbons which we shall now study is that they consist of two or more benzene rings which are linked to each other either directly or by an intervening aliphatic carbon group.

In synthesizing both the aliphatic and aromatic hydrocarbons we made use of the **Wurtz, Frankland, Fittig** and **Friedel-Craft** reactions for introducing an aliphatic radical in place of hydrogen of the original hydrocarbon, thereby forming a higher member of the homologous series.

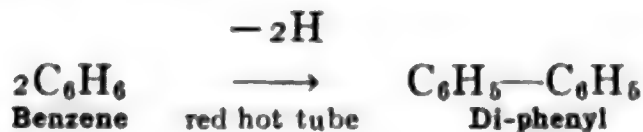


Di-phenyl.—If, however, instead of two aliphatic halides, or a benzene halide and an aliphatic, we use the benzene halide only, the same kind of reaction takes place with the formation of a hydrocarbon of the composition $C_{12}H_{10}$. Just as ethane is di-methyl so this compound must be di-phenyl.

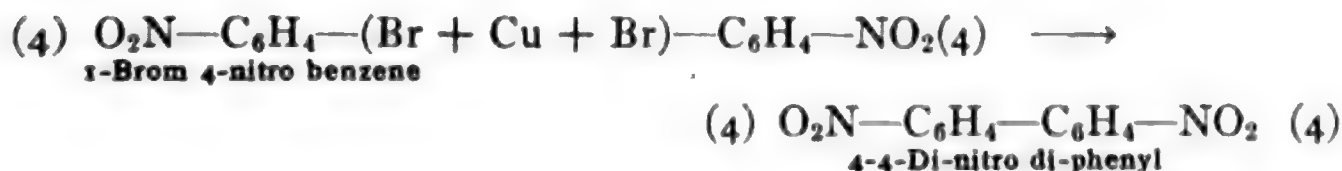




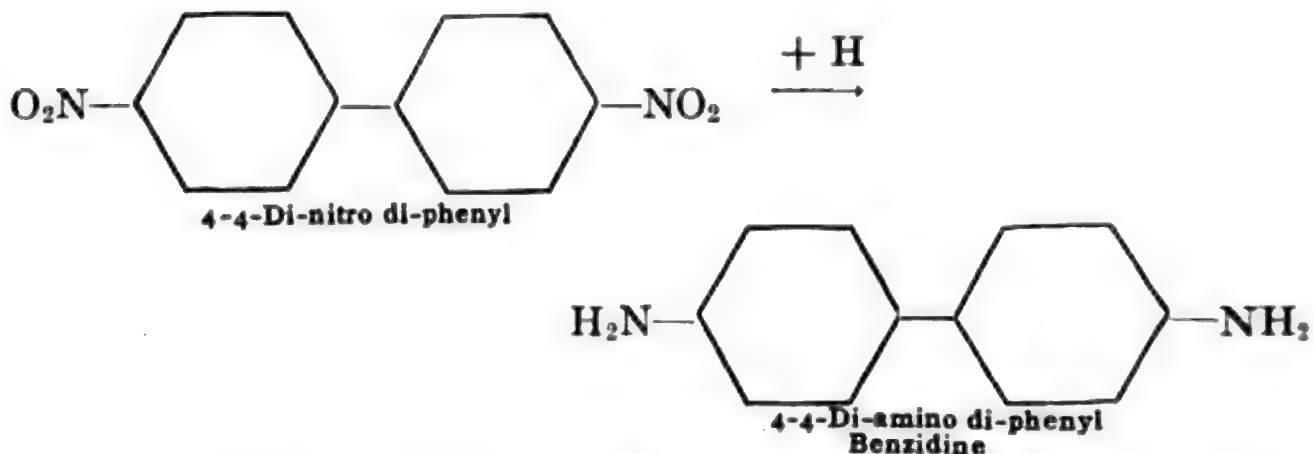
From Benzene.—It is possible to synthesize di-phenyl from benzene directly by a reaction that does not take place with aliphatic hydrocarbons. When the vapor of benzene is passed through a red hot tube di-phenyl is obtained, two atoms of hydrogen being lost.



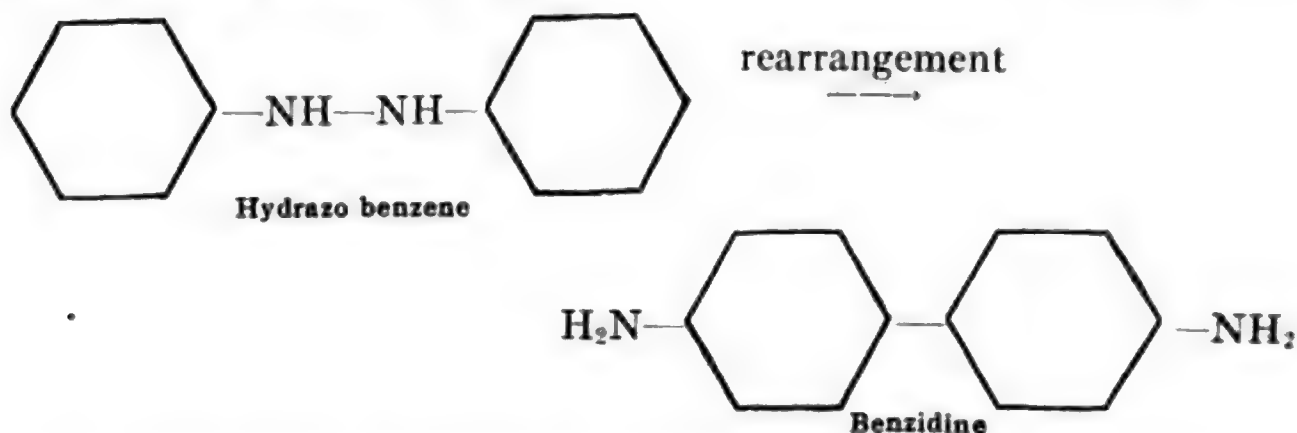
Di-nitro Di-phenyl.—Di-phenyl is present in the distillation products of coal tar probably resulting from the preceding reaction. It is a solid, crystalline compound; m.p. 71° , b.p. 254° . It acts like benzene in yielding halogen, nitro and sulphonic acid products by the direct action of halogens, nitric acid or sulphuric acid. In cases of direct substitution, when two groups enter the compound one enters each ring in the positions para to the linking carbon atoms. The **p-p-di-nitro di-phenyl** may also be prepared by heating **p-brom nitro benzene** with copper.



Benzidine.—This 4-4-di-nitro di-phenyl by reduction yields the corresponding 4-4-di-amino di-phenyl.

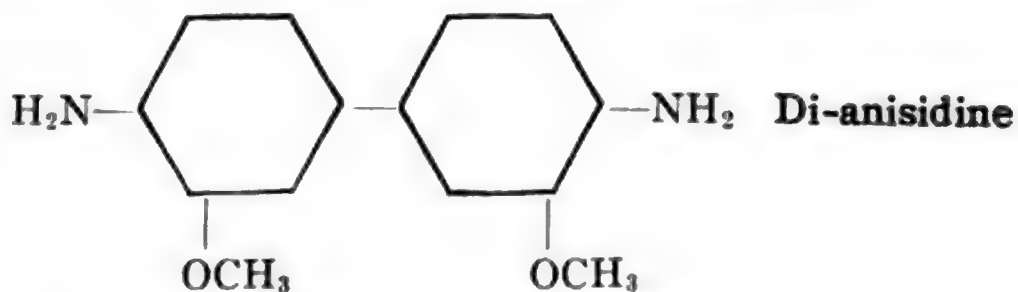


This 4-4-di-amino di-phenyl is **benzidine** which yields a very important group of dyes and which is formed by a molecular rearrangement from hydrazo benzene (p. 578).



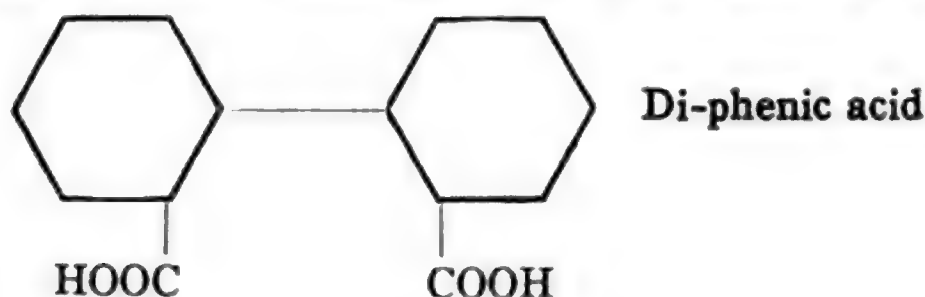
The diazotization of benzidine yielding *diazo* and *tetrazo* compounds, the coupling of these with phenols and amines yielding *azo* compounds, which are the **benzidine dyes**, should be recalled here (p. 569).

Di-anisidine.—A derivative of di-phenyl which is related to benzidine, and related also to **anisole**, $C_6H_5-OCH_3$ (p. 612) and to **anisdine**, $H_2N-C_6H_4-OCH_3$, is known as **di-anisidine**.



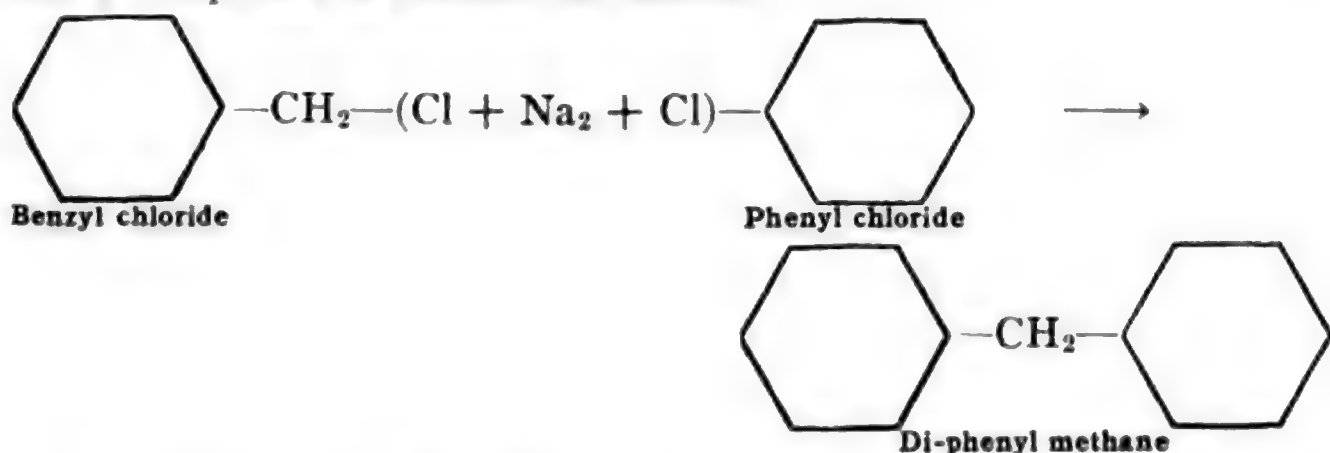
This also yields dyes of the benzidine class, an important one being **benzo sky blue**.

Di-phenic Acid.—A di-carboxy acid of di-phenyl in which the two carboxyls are both *ortho* to the ring linkage is of importance in connection with the constitution of another hydrocarbon, **phenanthrene**, which will be studied later (p. 806). It is known as **di-phenic acid**.



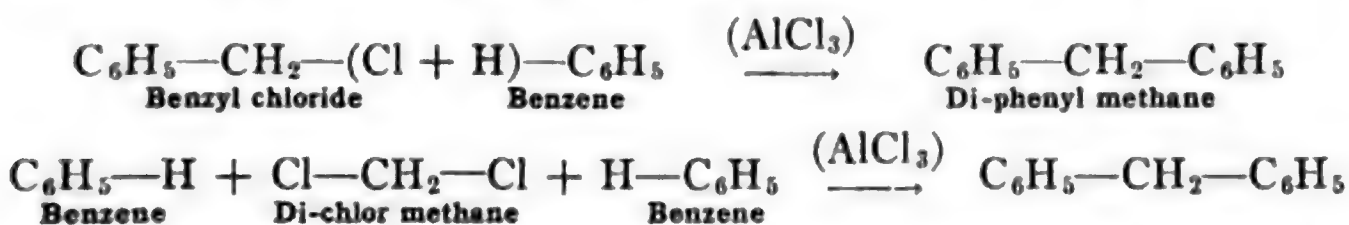
Di-phenyl Methane, $C_6H_5-CH_2-C_6H_5$

When **phenyl chloride** and **benzyl chloride** are treated with sodium the same kind of reaction takes place as in the formation of di-phenyl and a compound is obtained as follows:



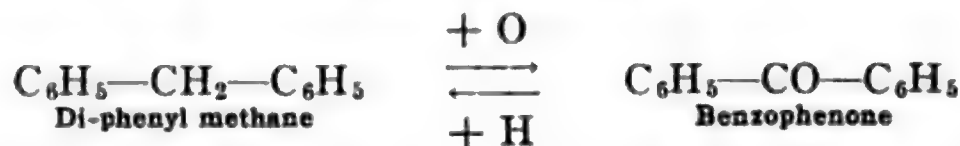
In this compound the *benzyl* group is linked to the *phenyl* group or the two benzene rings are linked by an intervening *methylene* group. Considering the methylene group as a residue of methane the compound is plainly **di-phenyl methane**. This is the name by which it is known.

By Friedel-Craft Reaction.—The best method of preparing the compound is by the **Friedel-Craft reaction** from benzene and benzyl chloride or by the same reaction from benzene and di-chlor methane.



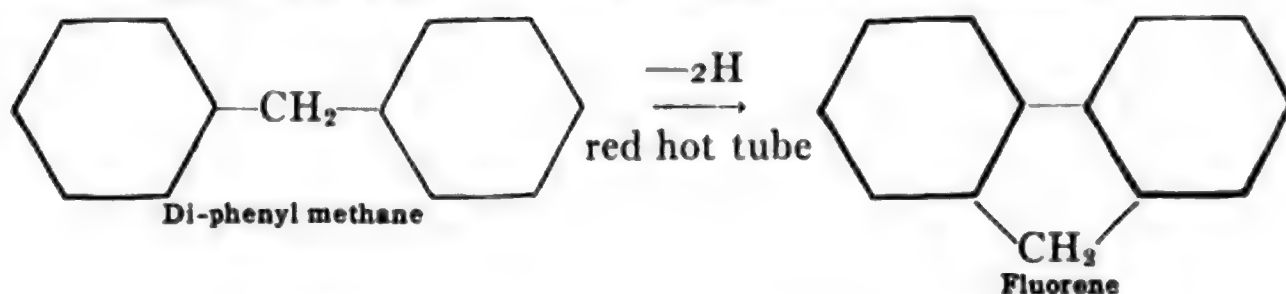
Benzophenone.—This last synthesis proves conclusively that it is a di-phenyl substituted methane. Di-phenylmethane is a crystalline

compound, m.p. 26° , with an odor of oranges. When it is oxidized the methylene group is affected with the replacement of the two hydrogens by one oxygen yielding **benzophenone** (p. 657).

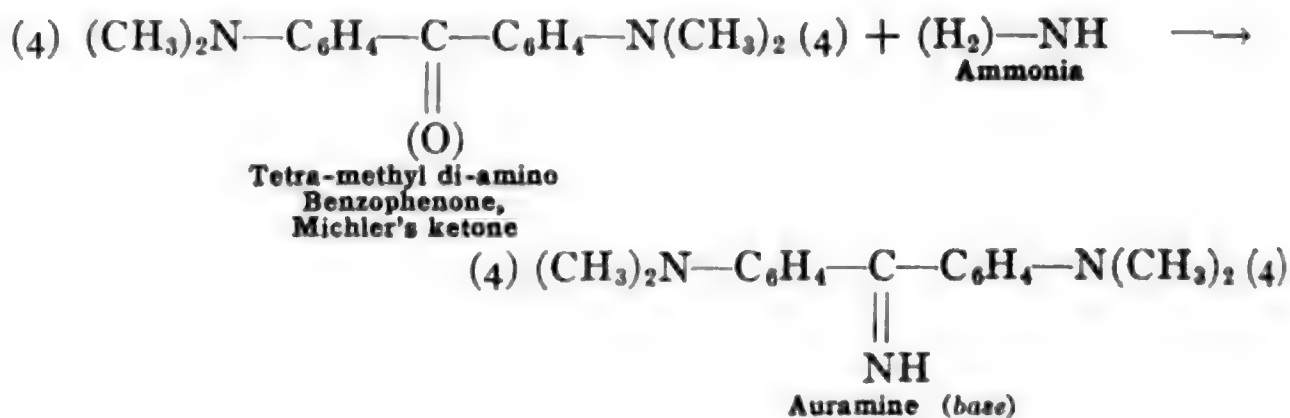


Conversely we may obtain the hydrocarbon from the ketone by reduction.

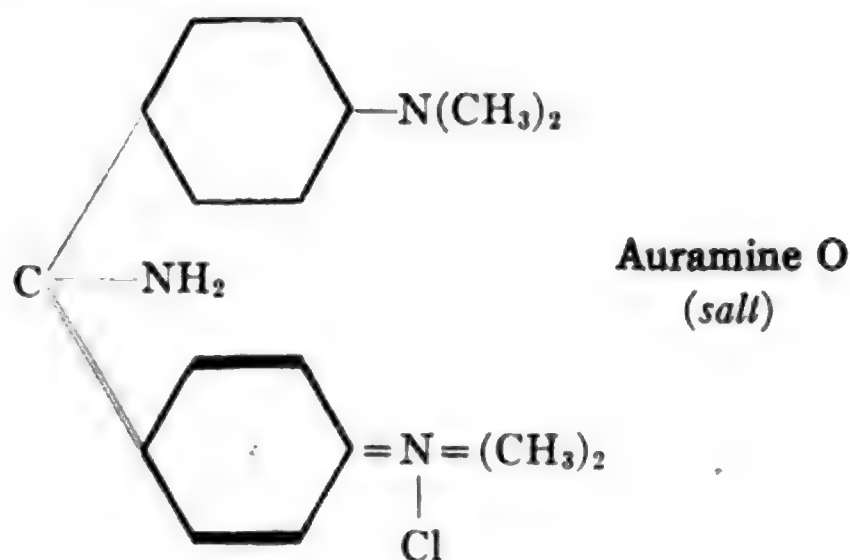
Fluorene.—We stated that when benzene is passed through a red hot tube two molecules lose two hydrogens with the formation of di-phenyl. Di-phenyl methane acts in the same way, one molecule losing two hydrogens, one from each ring from the positions *ortho* to the methylene linkage, the new hydrocarbon being known as **fluorene**.



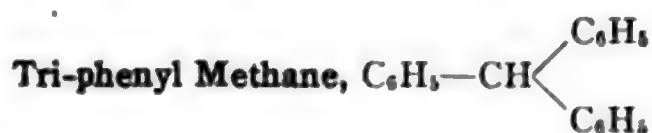
Dyes. Auramine.—A hydrocarbon which is very closely related to di-phenyl methane and which we shall study very soon is **tri-phenyl methane**. It is the mother substance of a large and very valuable group of dyes. While di-phenyl methane also yields dyes they are few in number. They are known as **auramine dyes**. The dye known as **auramine O** is made as follows: **Michler's ketone** (p. 667), which is **tetra-methyl di-amino benzo phenone**, is heated with ammonium chloride and anhydrous zinc chloride. The ammonium chloride yields ammonia which reacts with the ketone with the loss of water, the zinc chloride being the dehydrating agent.



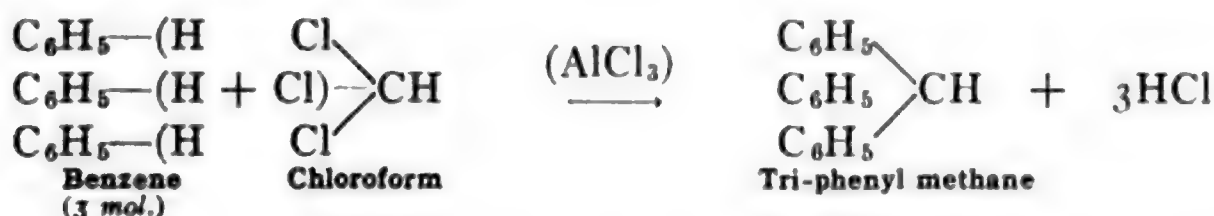
The auramine base as formed in this reaction is not itself a dye. The actual dye is the hydro-chloride salt.



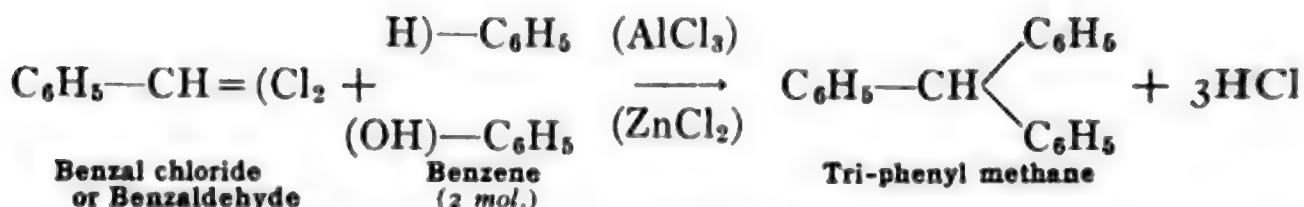
The discussion of the constitution of this and related dyes will be taken up with the **tri-phenyl methane dyes**. **Di-phenyl ethane**, the next higher homologue analogous to di-phenyl methane, is also known in isomeric forms similar to the symmetrical di-chlor ethane or ethylene chloride and the unsymmetrical di-chlor ethane or ethylidene chloride.



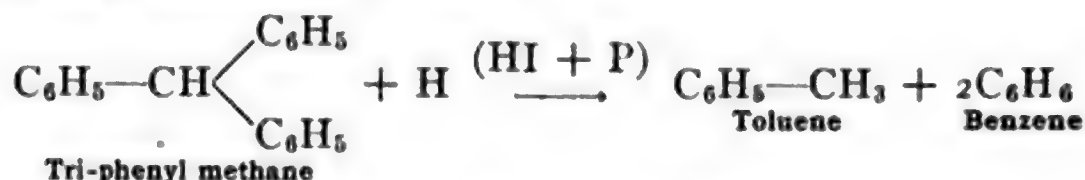
Synthesis.—This hydrocarbon is by far the most important of those in which two or more benzene rings are linked together by intervening aliphatic carbon groups. Just as methyl chloride and benzene by the **Friedel-Craft reaction** yield **phenyl methane** (methyl benzene or toluene); and methylene chloride, di-chlor methane, with benzene yields **di-phenyl methane**; so by the same reaction **tri-chlor methane**, **chloroform**, yields with **benzene** a hydrocarbon which by this synthesis must be **tri-phenyl methane**.



It may be synthesized also from **benzal chloride** and **benzene** by the **Friedel-Craft reaction**, or from **benzaldehyde** and **benzene** by heating with anhydrous zinc chloride to $250^\circ\text{—}270^\circ$.



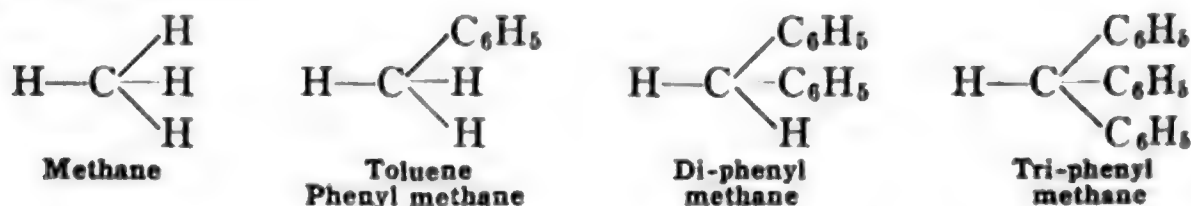
Tri-phenyl methane is a solid crystallizing in various forms, m.p. 92° , b.p. 358° . It is quite easily soluble in ether or benzene but only slightly in alcohol. When reduced by means of phosphorus and hydriodic acid it yields **benzene** and **toluene**.



TRI-PHENYL METHANE DYES

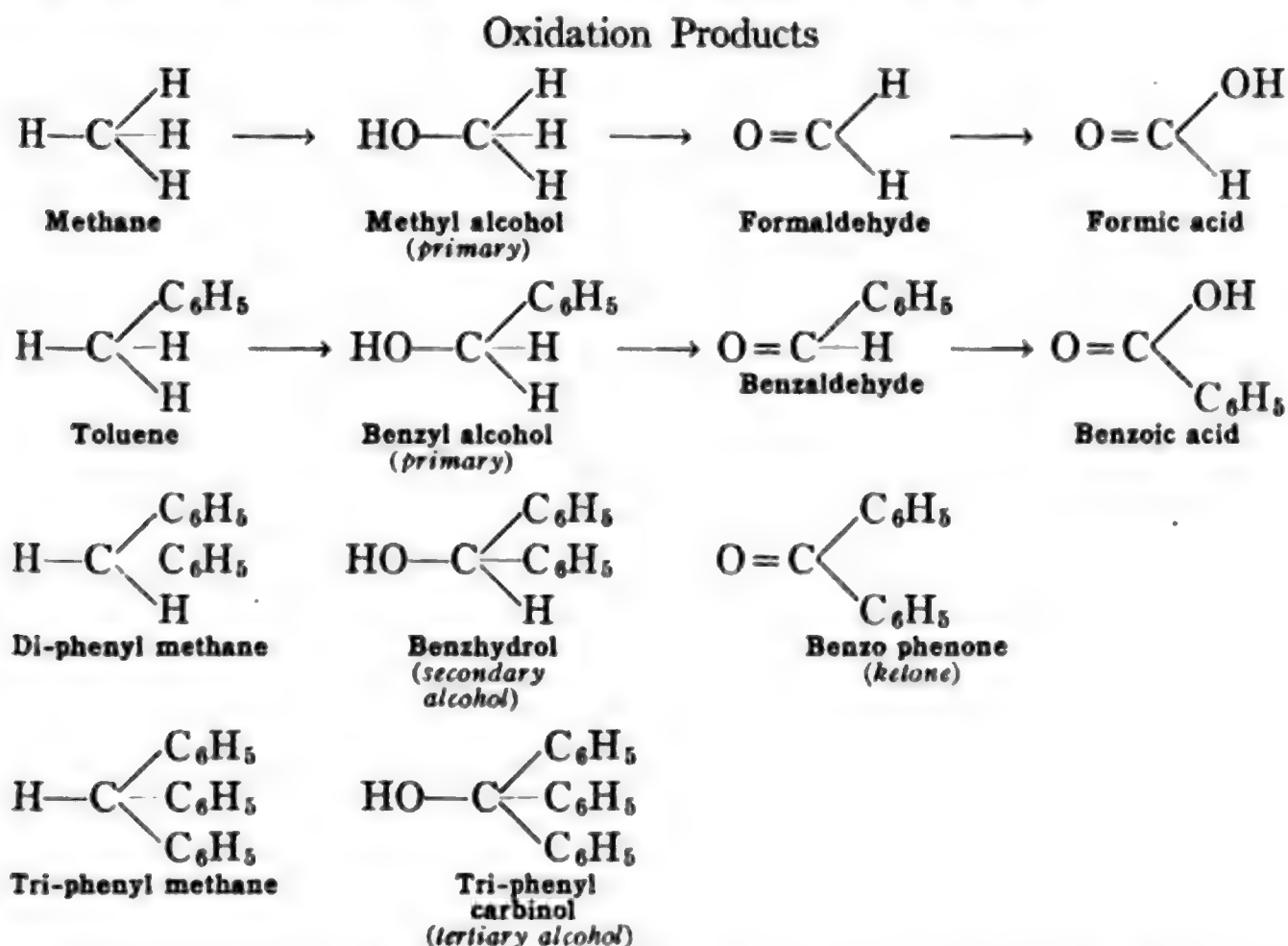
The importance of tri-phenyl methane is in its relation to a large number of very valuable dyes which are known as the **tri-phenyl methane dyes** and which include several smaller groups known as the **rosaniline**, **para-rosaniline**, **malachite green**, **rosolic acid** and **phthalein dyes**. The relationship between these dyes and tri-phenyl methane has been worked out in an exceedingly interesting manner. We shall not, however, attempt to present the matter in its historical connection but will show the steps in the relationships as they have been worked out at various times, disregarding altogether any chronological sequence in their order.

Methane Character.—Tri-phenyl methane is the hydrocarbon mother substance from which the dyes are derived. The relation between the hydrocarbons, **methane**, **toluene**, **di-phenyl methane** and **tri-phenyl methane** is clearly seen if we write their formulas as derivatives of methane.



Oxidation Products.—Methane stands at one end, as a pure *aliphatic* hydrocarbon, while the others are phenyl derivatives becoming more strongly *aromatic* in character, but retaining, even in tri-phenyl methane, at least one methane hydrogen. Thus toluene, di-phenyl methane and tri-phenyl methane exhibit, in the order given, a grad-

ually decreasing aliphatic character. This is most clearly shown in the oxidation products which may be presented as follows:



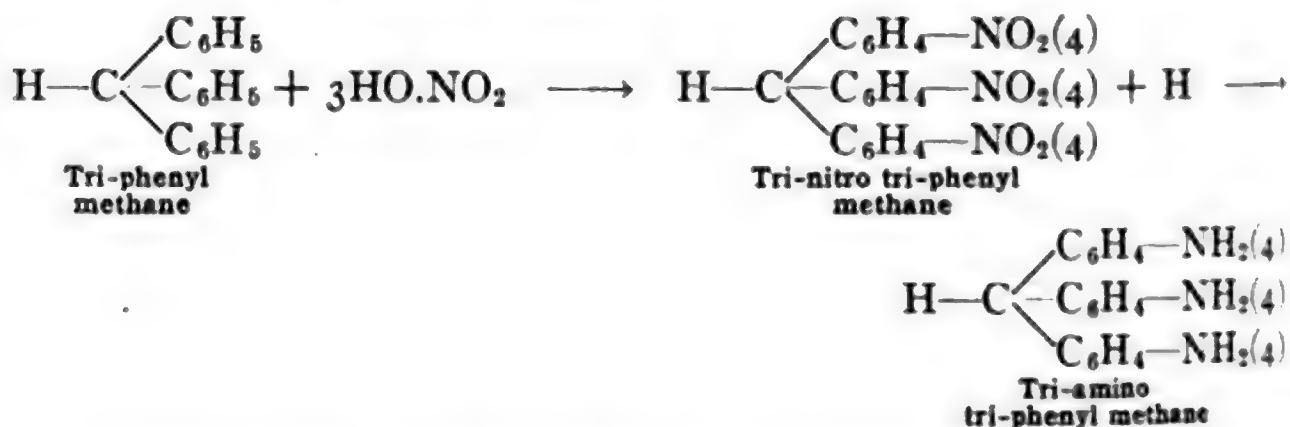
These relationships are exactly analogous to those between primary, secondary and tertiary hydrocarbons and alcohols (Part I, p. 123). The first two, viz., methane and toluene, are *primary* hydrocarbons each containing a carbon with three remaining hydrogens linked to it. They yield primary alcohols, aldehydes and acids. Di-phenyl methane is a *secondary* hydrocarbon containing only two remaining hydrogen atoms linked to the aliphatic carbon and it yields a secondary alcohol and a ketone. The fourth, tri-phenyl methane, is a *tertiary* hydrocarbon containing one hydrogen only, which is linked to the aliphatic carbon, and therefore it is capable of oxidation only to a tertiary alcohol or *carbinol*. The relation of this carbinol to the hydrocarbon and its derivatives we shall find to be very important.

Benzene Character.—The three hydrocarbons which contain benzene rings, viz., toluene, diphenyl methane and tri-phenyl methane, all act *like benzene* and yield characteristic benzene derivatives. Those of especial importance are the *nitro* and *amino* ring substitution products.

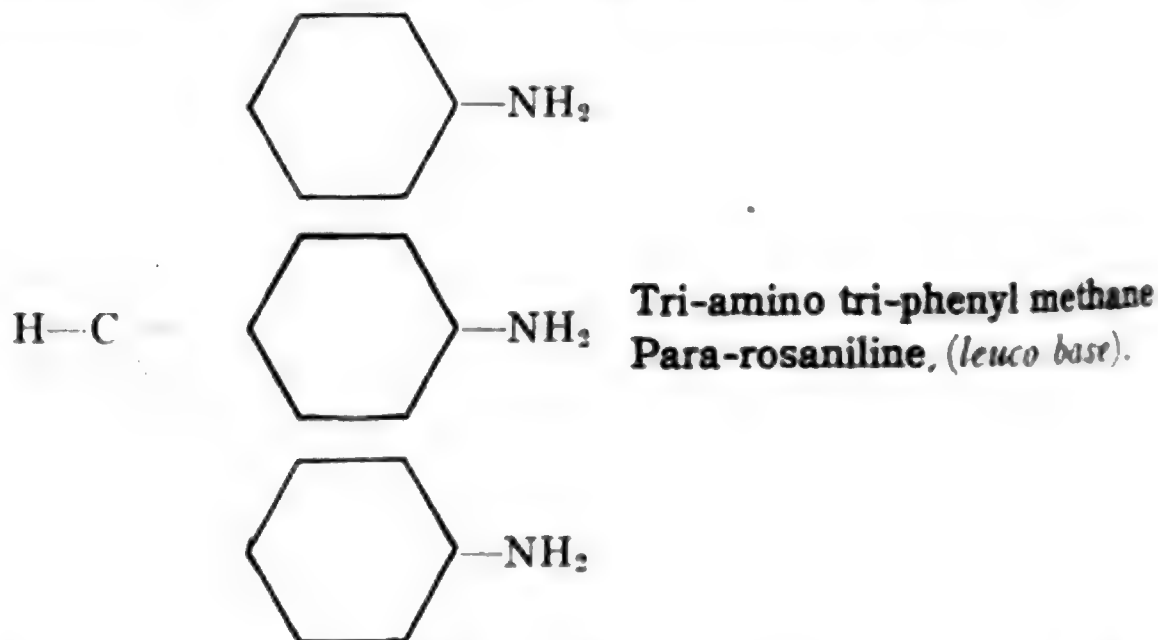
Para-rosaniline

Tri-nitro Tri-phenyl Methane.—When tri-phenyl methane is nitrated a tri-nitro tri-phenyl methane is obtained in which one nitro group enters each benzene ring.

Tri-aminoTri-phenyl Methane.—This on reduction passes to the corresponding tri-amino tri-phenyl methane.

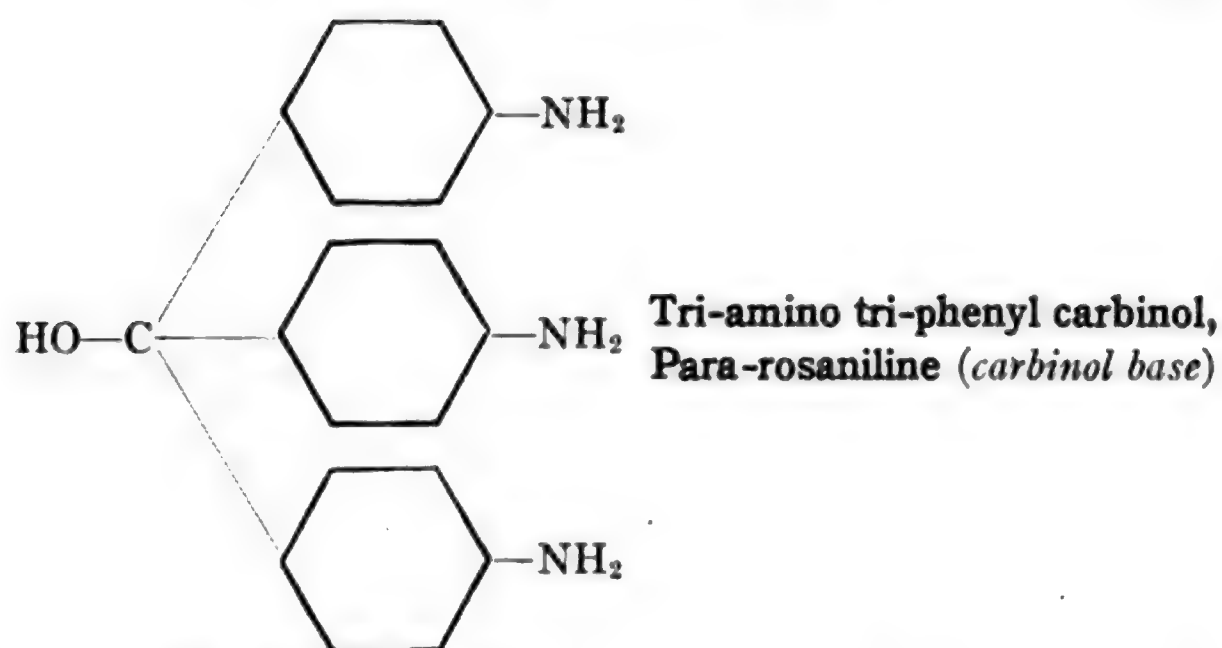


Furthermore, it has been shown that the three nitro and the three amino groups are in the *para* positions in the benzene rings. The full structural formula for the tri-amino tri-phenyl methane is, therefore,

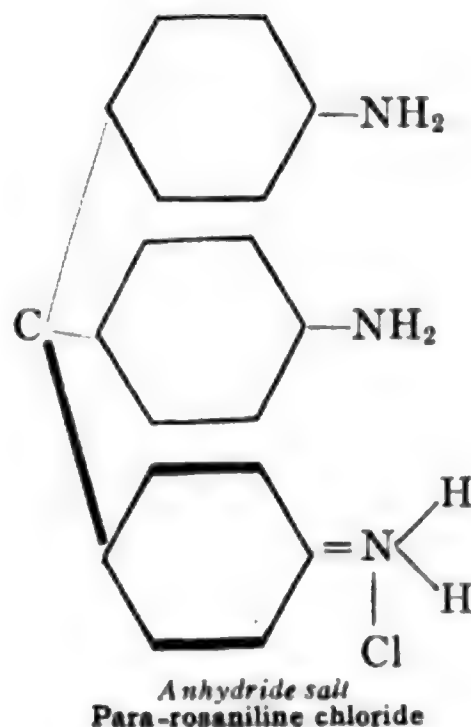
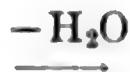
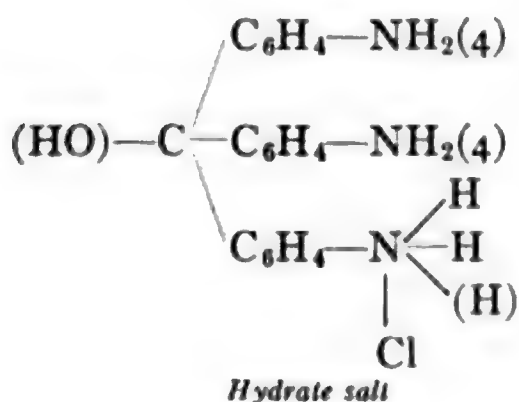
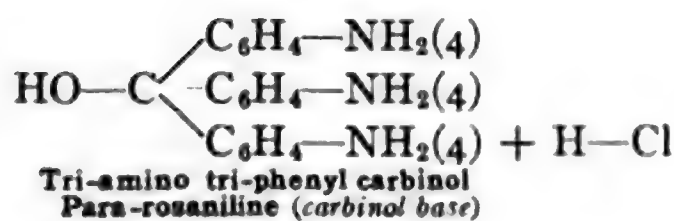
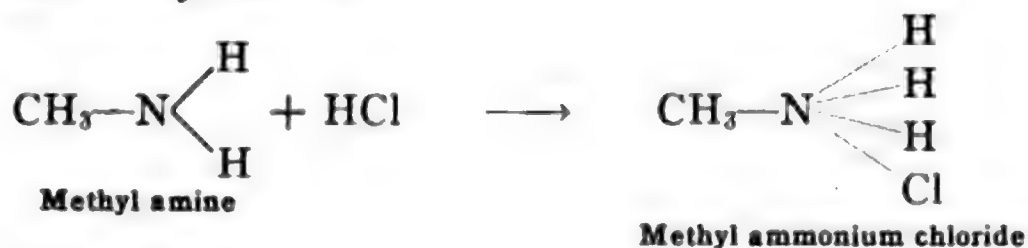


Para-rosaniline, Leuco Base.—This compound, viz., the *p*-tri-amino derivative of the hydrocarbon tri-phenyl methane, is the more immediate mother substance of a dye known as **para-rosaniline**. It is termed the *leuco base* of the dye.

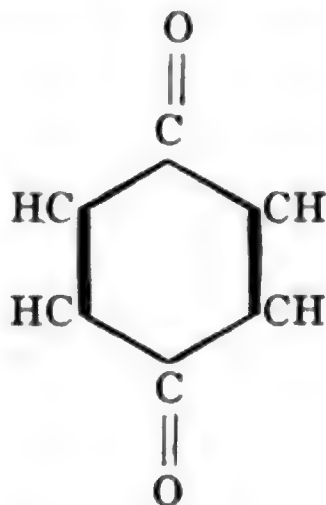
Tri-amino Tri-phenyl Carbinol. Carbinol Base.—When tri-amino tri-phenyl methane is oxidized it yields a carbinol or alcohol just as tri-phenyl methane itself does, viz.,



Para-rosaniline Chloride.—This carbinol is known as para-rosaniline, *carbinol base*. It is not a dye but when treated with acids it yields salts which are colored and which possess the properties of dyes. These salts result from one of the amino groups reacting with the acid, forming an ammonium salt, the *tri-valent* nitrogen of the amine becoming *penta-valent* in the salt, as in the formation of methyl ammonium chloride from methyl amine.



In the above reaction there is first formed, in the cold, a hydrate salt which is *colorless*. This on heating loses water, as indicated, yielding an *anhydride salt* which is the *dye* and has the constitution as given. The formation of this anhydride dye salt involves the conversion of one of the benzene rings from the normal structure with alternate double and single bonds to a structure found in **quinone** (p. 636).



Quinoid Structure of Dyes.—This is known as the quinone or *quinoid structure* and, according to theories regarding the relation between constitution and color in compounds possessing properties of dyestuffs, it is the presence of a group with this structure which endows the dyes of this and related classes with color.

Chromophore.—Such a group is termed a *chromophore* and each large group of dyes has a characteristic chromophore.

Considering again what we have brought out in connection with para-rosaniline we should note that there are four distinct compounds, viz., the *amine base* or *leuco base*, the *carbinol base*, the *hydrate salt* and the *anhydride salt* or *dye*. Now these four types of compounds are known not only in the case of para-rosaniline but in the case of all tri-phenyl methane dyes. The general characters of these four types of tri-phenyl methane derivatives, including their color properties which are very important, may be given as follows:

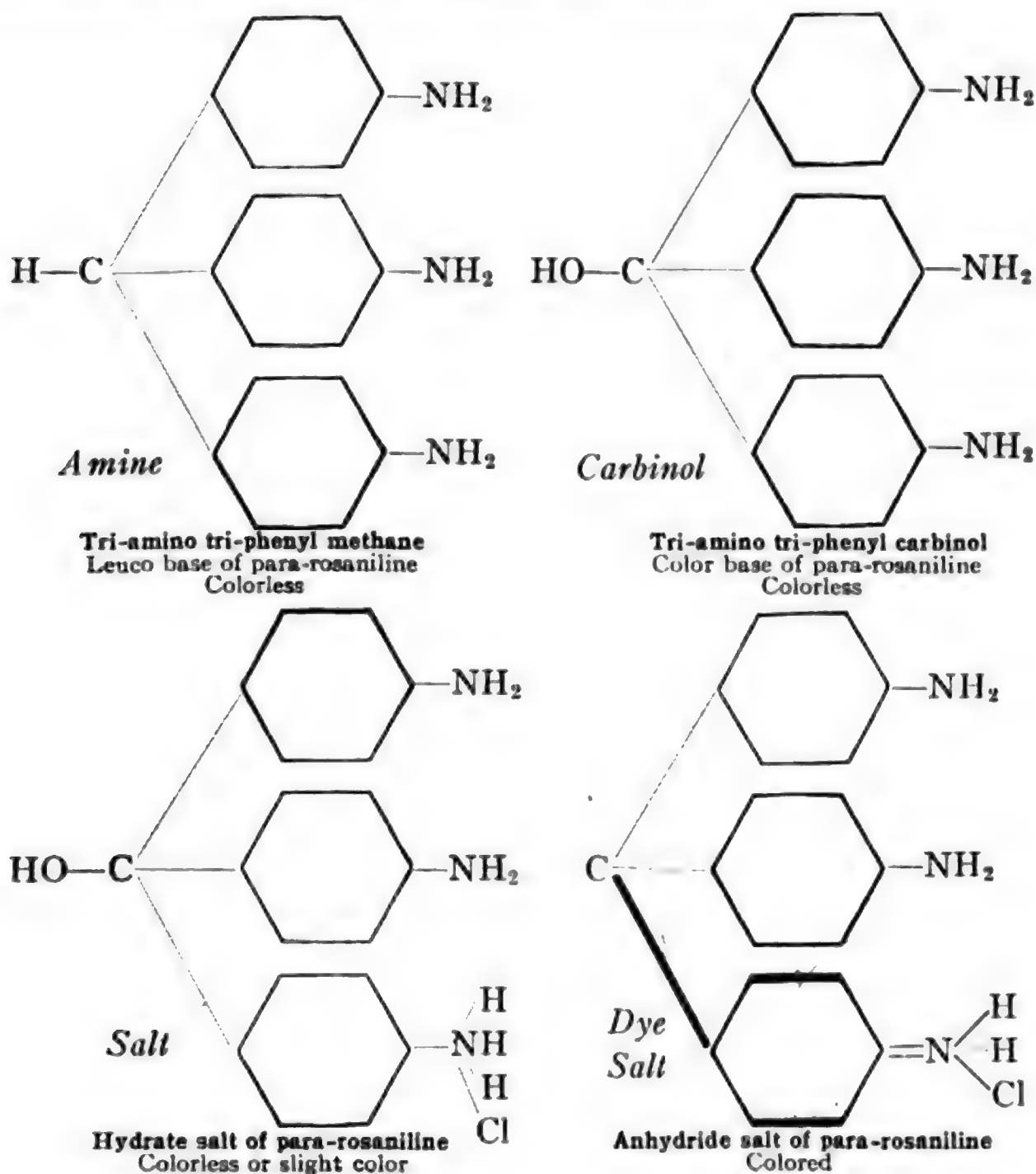
Leuco Base.—(1) The *amine base* is the simple amine substitution product of the hydrocarbon tri-phenyl methane. It may be obtained by reducing the other compounds and is thus the reduction product. It is *colorless* and is termed the *leuco base*, the word *leuco* meaning colorless.

Carbinol Base.—(2) The *carbinol base* is the alcohol or hydroxyl

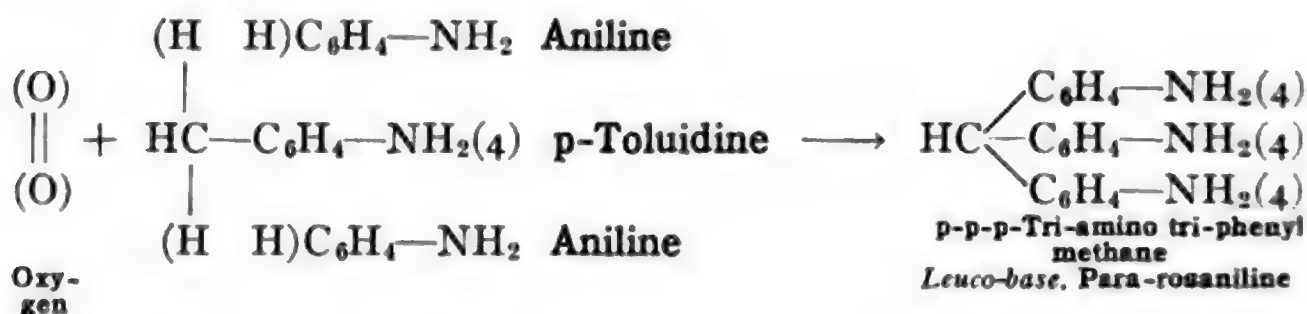
compound resulting from the oxidation of the amine base. It is usually *colorless* and is termed the *color base* or *carbinol base*.

Colorless Hydrate Salt.—(3) The *hydrate salt* is formed from the carbinol base by addition of acid. It is colorless or with slight color. It may be present in the cold solution but on heating readily loses water yielding the last form.

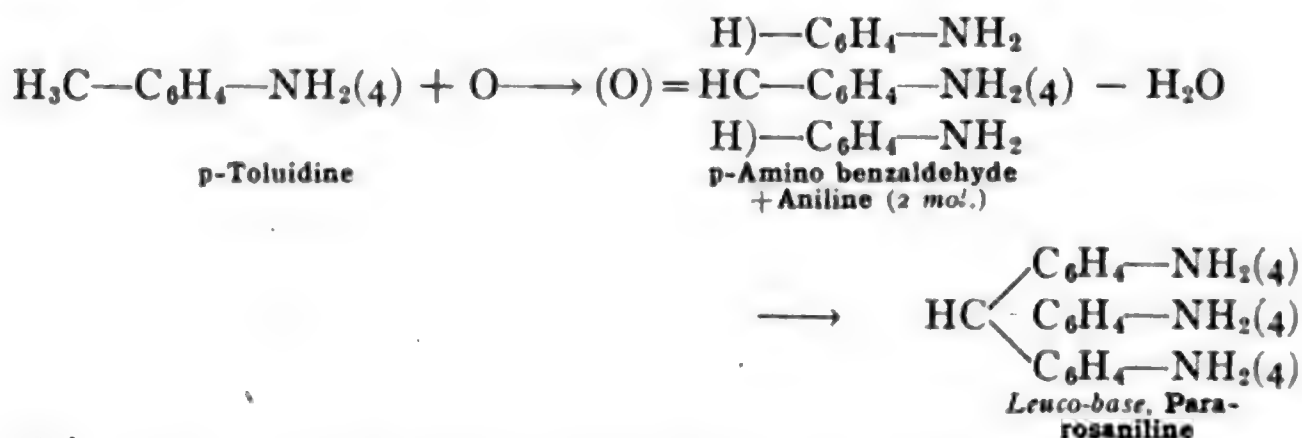
Colored Dye Salt.—(4) The *anhydride salt* formed by loss of water from the hydrate salt. It has the *quinoid structure* in the benzene ring linked to the ammonium salt group. This compound is *colored* and is the *dye salt* or the actual *dye*. The formulas of the para-rosaniline compounds may be given all together as follows:



Preparation of Para-rosaniline.—The synthesis of pararosaniline as we have given it, viz., in outline, from tri-phenyl methane—→tri-nitro tri-phenyl methane,—→tri-amino tri-phenyl methane,—→tri-amino tri-phenyl carbinol—→colorless hydrate salt—→anhydride salt or dye, was developed during the study of the constitution of the compound and establishes its constitution as we have given it. This synthesis is not, however, a practical one for the commercial preparation of the dye. The method now used is in effect the same as was used in the discovery of the substance though its explanation is the result of the constitutional study which led to the synthesis above. When *two molecules* of aniline and *one molecule* of p-toluidine are treated with an oxidizing agent, e.g., arsenic oxide chromic acid, or mono-nitro benzene, the leuco base of para-rosaniline is obtained. In the light of the constitution of the leuco base as we have given it the reaction may be represented as follows:



It is probable that the reaction proceeds in two steps: first, the p-toluidine has the methyl group oxidized to the aldehyde group yielding p-amino benzaldehyde; second, this aldehyde then reacts with aniline just as benzaldehyde does with benzene in the synthesis of tri-phenyl methane (p. 735).



It is clear that the aliphatic carbon atom of the leuco base is the ali-

phatic methyl carbon atom of *p*-toluidine. That this methyl carbon in toluidine is *para* to the amino group is in agreement with the constitution of the leuco base and with the fact that *p*-toluidine will thus yield the leuco base while *o*-toluidine will not. The conversion of the leuco base into the dye salt is accomplished by further oxidation to the carbinol base and treatment of this with acid and heat yielding the anhydride salt or dye. These reactions need not be repeated.

An interesting historical fact is that the original preparation of the dye was by the oxidation of crude aniline alone. Then it was shown that pure aniline did not yield the dye and that the crude compound, which did yield the dye, always contained *p*-toluidine also. Thus the latter compound is absolutely essential to the synthesis. The original crude preparation, the synthetic commercial preparation and the synthesis from tri-phenyl methane all agree and are in accord with the established constitution. The name **para-rosaniline** was given to the dye because *para*-toluidine is an essential synthetic constituent.

Rosaniline

When the dye that was made by oxidizing crude aniline was studied and the facts which we have stated were determined, it was also found that the dye was not one compound but that two were present as a mixture. Originally the mixture of the two was called simply rosaniline, but to distinguish the two compounds the one we have been studying because of its relation to *para*-toluidine is called **para-rosaniline** while the other is named simply **rosaniline**. Sometimes the name rosaniline is applied to the former and the latter is then called homorosaniline. The first names are the better and are now generally adopted.

Rosaniline then is another dye compound related to *para*-rosaniline. It is not isomeric but differs in composition by CH_2 . This at once suggests that it is a homologue and such has been found to be the case. Its constitution has been established by its synthesis from pure compounds. When, instead of using two molecules of aniline and one molecule of *p*-toluidine as in the synthetic preparation of *para*-rosaniline, we use *one molecule each* of **aniline**, ***p*-toluidine** and **ortho-toluidine** then we obtain the leuco base of **rosaniline** alone. From the leuco base the dye salt is obtained by the usual methods. The reactions analogous to the ones for *para*-rosaniline are:

toluidine, found that when crude aniline was oxidized with chromic acid a colored product was obtained which he succeeded in isolating as a rose-violet dye and to which he gave the name **mauve**. The process was patented in England and the dye was made and used for a considerable time. At present it is not made or used to any extent. This dye **mauve** was the first *aniline dye* or chemically prepared dye to be made and its discovery and commercial preparation mark an epoch in industrial chemistry and the beginning of what is usually termed the *aniline dye industry*. The branch of industrial chemistry thus opened is perhaps without a parallel in the variety, usefulness and value of the products obtained. The recognition of the importance of the discovery was made in 1906, on its 50 year anniversary, by a Jubilee Celebration in England, America and Germany at which the discoverer was honored and congratulated by various societies especially the Society of Chemical Industry of England and America, The American Chemical Society and Die Deutsche Chemische Gesellschaft.

Perkin Medal.—The American Society of Chemical Industry established a medal known as **The Perkin Medal** the first impression of which was presented to **Sir Wm. Perkin** in person. The medal is now awarded annually to the American chemist who has contributed the most important work on industrial chemistry. The men who have been awarded the medal, up to 1921, are the following:

- 1906 **Sir William Perkin**; The Discovery of Mauve, the First Aniline Dye.
- 1908 **J. B. F. Herreshoff**; Contact Process for Sulphuric Acid.
- 1909 **Arno Behr**; Corn Products Industry.
- 1910 **E. G. Acheson**; Carborundum and Artificial Graphite.
- 1911 **Charles M. Hall**; Aluminium.
- 1912 **Herman Frasch**; Desulphurized Petroleum and Louisiana Sulphur.
- 1913 **James Gayley**; Dry Blast Iron Smelting.
- 1914 **John W. Hyatt**; Celluloid and Flexible Roller Bearings.
- 1915 **Edward Weston**; Contributions to Electro Chemical Industry.
- 1916 **L. H. Baekeland**; Photography, Electro Chemistry and Plastics (Velox and Bakelite).
- 1917 **Ernest Twitchell**; Fats, Soap and Glycerol.
- 1918 **Auguste J. Rossi**; Titanium and Titaniferous Iron Ores.
- 1919 **Frederick G. Cottrell**; Electrical Precipitation of Suspended Particles.
- 1920 **Charles F. Chandler**; General Industrial Chemistry.
- 1921 **Willis R. Whitney**; Industrial Research.

The dye **mauve** is not a tri-phenyl methane compound and so does

not belong to the same group of dyes as do the rosanilines but its discovery led to investigations from which the latter dyes resulted.

Fuchsin, Magenta.—In 1859 **Verguin** in France found that crude aniline oxidized by means of stannic chloride yielded a red dye which was named **fuchsin** and also **magenta**. Other oxidizing agents were used later, *e.g.*, mercuric chloride, arsenic acid, mono-nitro benzene.

Hofmann.—In 1862 **Hofmann**, whose name is always associated with the development of our ideas in regard to the constitution of amines, showed that the red dye obtained was a salt of a base which he named **rosaniline** and later that *p*-toluidine, always a constituent of crude aniline, was essential to the formation of the dye.

Fischer.—Later **Emil and Otto Fischer**, the former being the one to whom we have repeatedly referred in connection with uric acid, carbohydrates and proteins, proved that the constitution of para-rosaniline was as we have previously given it and developed the methods of synthesis.

Caro, Rosenstiehl, Schorlemmer, Hantzsch, Nietski.—A few other chemists whose names belong in any list of those who have developed the aniline dye industry may also be mentioned. The first three were concerned principally with the dyestuff industry, while the last two developed theories in regard to the relationship between constitution and color in dye compounds.

The rosaniline dye first obtained was probably a mixture of salts of both para-rosaniline and rosaniline. The names given to it at the beginning, viz., **fuchsin** and **magenta**, are still used. **Acid fuchsin**, a common form of the dye, is a mixture of the sodium salts of the mono- and di-sulphonic acid derivatives of para-rosaniline and rosaniline.

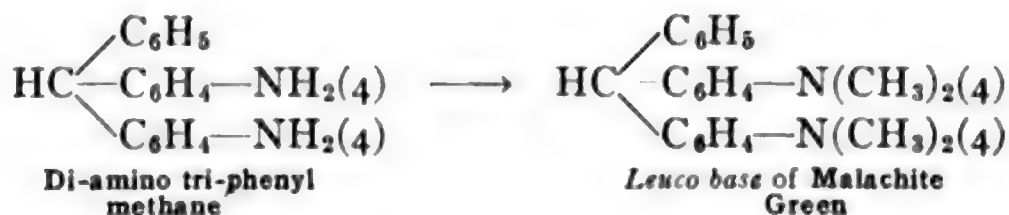
Formaldehyde and Phosgene Methods.—Two other processes for the commercial preparation of fuchsin are the **formaldehyde** and the **phosgene**, COCl_2 , processes. For details in regard to them special books on dyes should be consulted, *e.g.*, **Cain & Thorpe**.

Synthetic Dyes.—In common usage the term *aniline dye* is applied to any dyestuff prepared from organic chemical substances. As the first dye made and many of those made at present are derived from aniline the above name is significant. It is not a true name, however, in many cases for though some of the *azo* and *benzidine dyes* (p. 573) may be considered as aniline derivatives those derived from **naphthalene** can not be so considered. Other dyes which we shall study later,

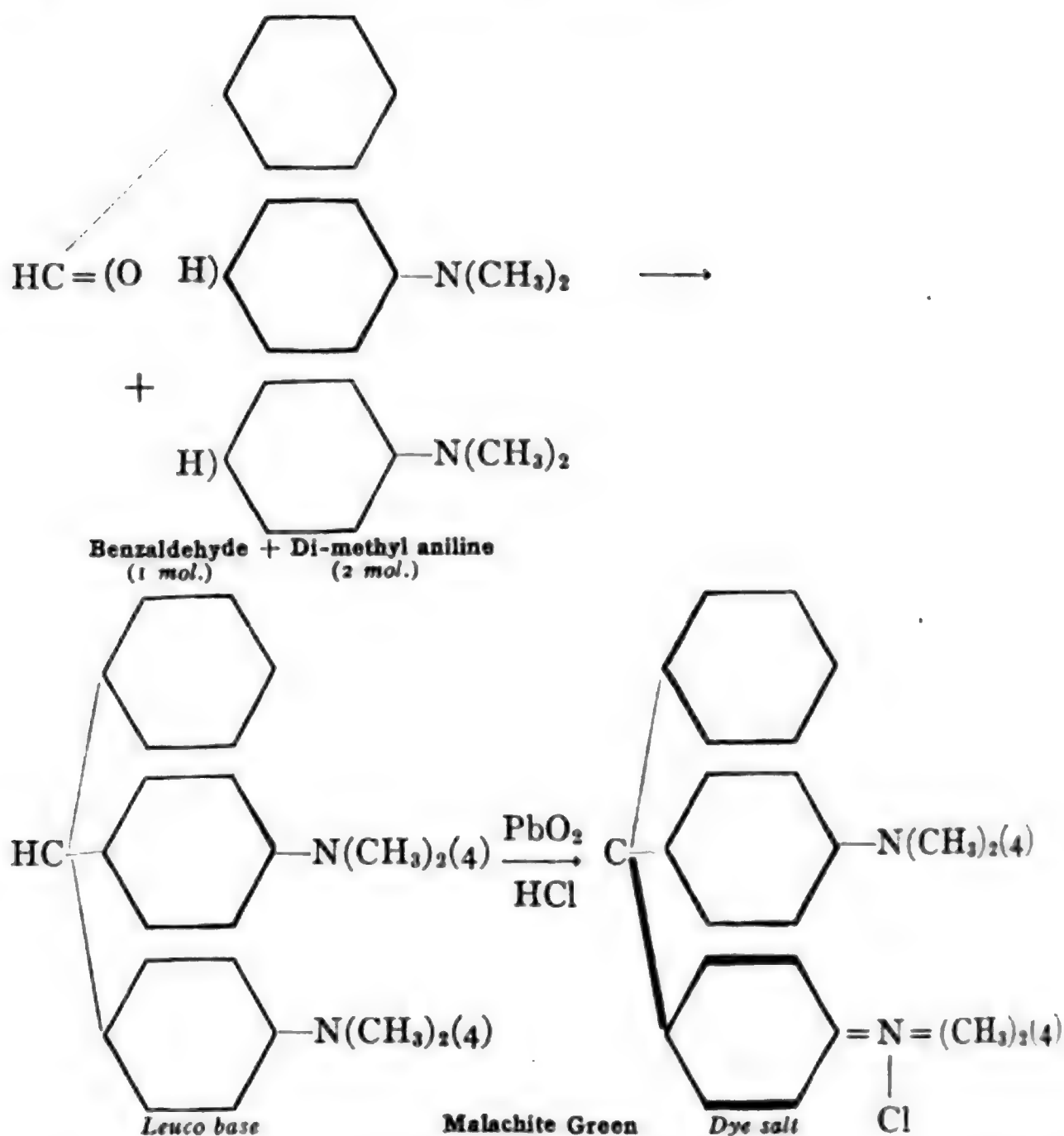
e.g., **alizarin**, are in no sense aniline products. All of the compounds from which the chemical dyes are made are, however, obtained either directly or indirectly from **coal tar** (p. 494), and the name *coal tar dyes* is better than aniline dyes in designating the entire class. The name *chemical dyes* is also sometimes used but the best name on the whole is *Synthetic Dyes* as including any dyestuff made by chemical processes and not from a natural plant source, *e.g.*, natural **indigo**, **turkey red**, etc., or animal source, *e.g.*, **cochineal** or natural **Tyrian purple**. Such a name might be taken to include inorganic coloring substances but the term *dye* is restricted to organic compounds with color which color is able to be fixed upon animal or vegetable fibers. The synthetic dyes include colors of practically every conceivable tint or shade and in their technical treatment for dyeing fibers are of various groups. Further discussion of the general subject of dyes is not desirable in this text but may be found in special works on the subject as mentioned in the list of references (p. 910).

Malachite Green

Another group of dyes belonging to the tri-phenyl methane series but which differ from the rosanilines in not being derived from *tri-amino* tri-phenyl methane is represented by **malachite green**. It is one of the oldest of the synthetic dyes, having been first prepared by **O. Fischer** in 1877. The immediate mother substance is **di-amino tri-phenyl methane** of which the leuco base of the dye is the tetramethyl derivative.



It is prepared as follows: **Di-methyl aniline**, *two molecules*, and **benzaldehyde**, *one molecule*, are heated with zinc chloride or hydrochloric acid. Condensation with the loss of water takes place and the *leuco base* of malachite green is obtained. The oxidation of the leuco base to the *carbinol base* is accomplished with **lead peroxide**, PbO_2 .

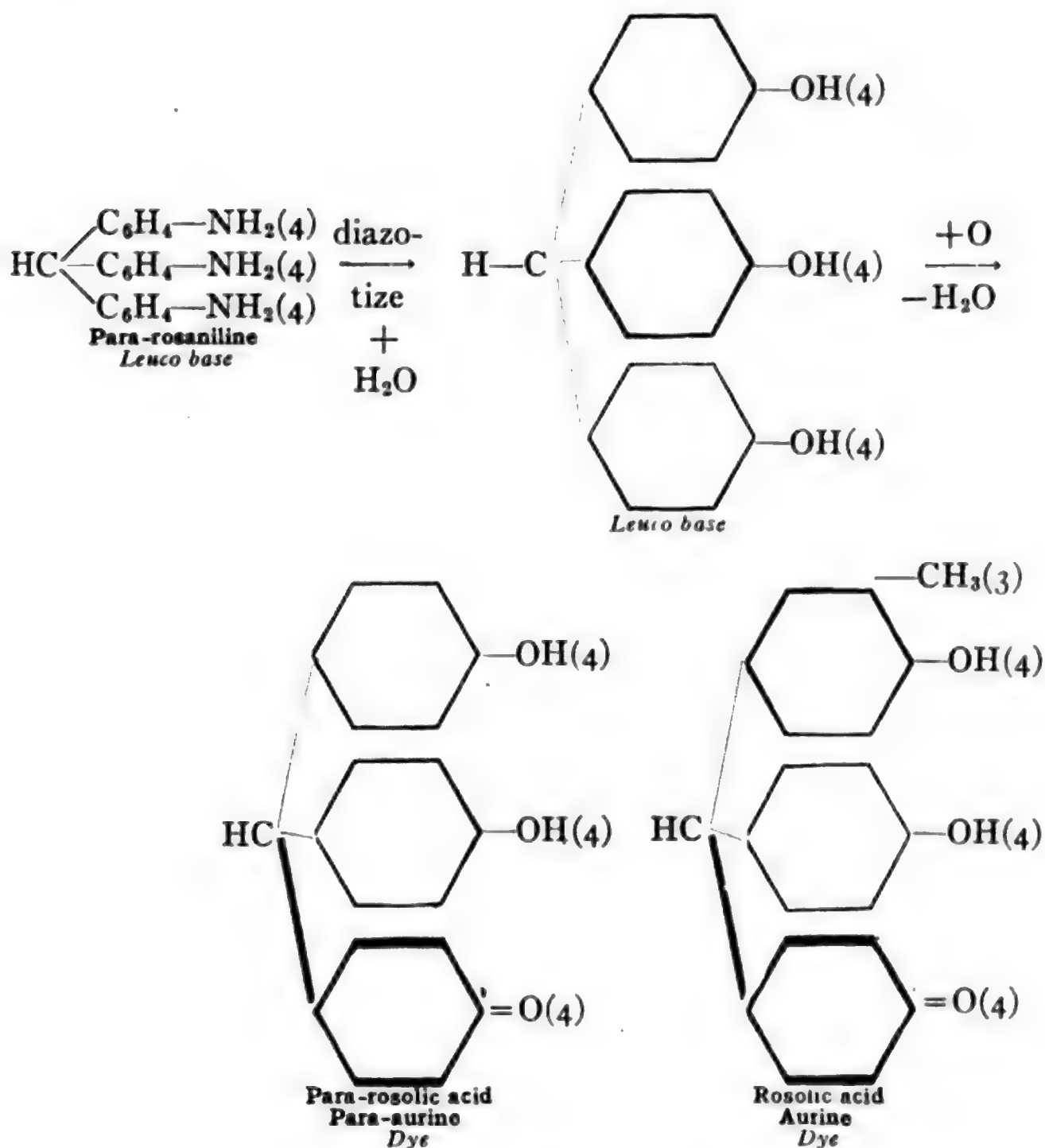


The dye salt may be obtained as the chloride or acetate but usually in beautiful green crystals of the oxalate or as the double chloride with zinc. Other derivatives corresponding to malachite green are dyes of various shades of green and blue.

Rosolic Acid

A third group of dyes belonging to the tri-phenyl methane series yet differing from both rosaniline and malachite green is the **rosolic acid** group which are known as **aurines**. Two dyes are known analogous to para-rosaniline and rosaniline. They are **para-rosolic acid** and **rosolic acid**, the latter being the methyl substitution product of the former.

The leuco base of para-rosolic acid is the **tri-hydroxy tri-phenyl methane** as is proven by its formation from para-rosaniline leuco base by diazotizing and then decomposing the diazo compound with water (p. 597).



The dye compound which, strictly speaking, is not a salt but a quinone is obtained directly by oxidizing the leuco base, the intermediate carbinol losing water without the action of an acid. Dyes of this group are not very numerous, rosolic acid itself being used chiefly as an indicator. It is interesting that the compound was prepared long before **Perkin**, **Hofmann** and **Fisher** made the first actual synthetic dye and established

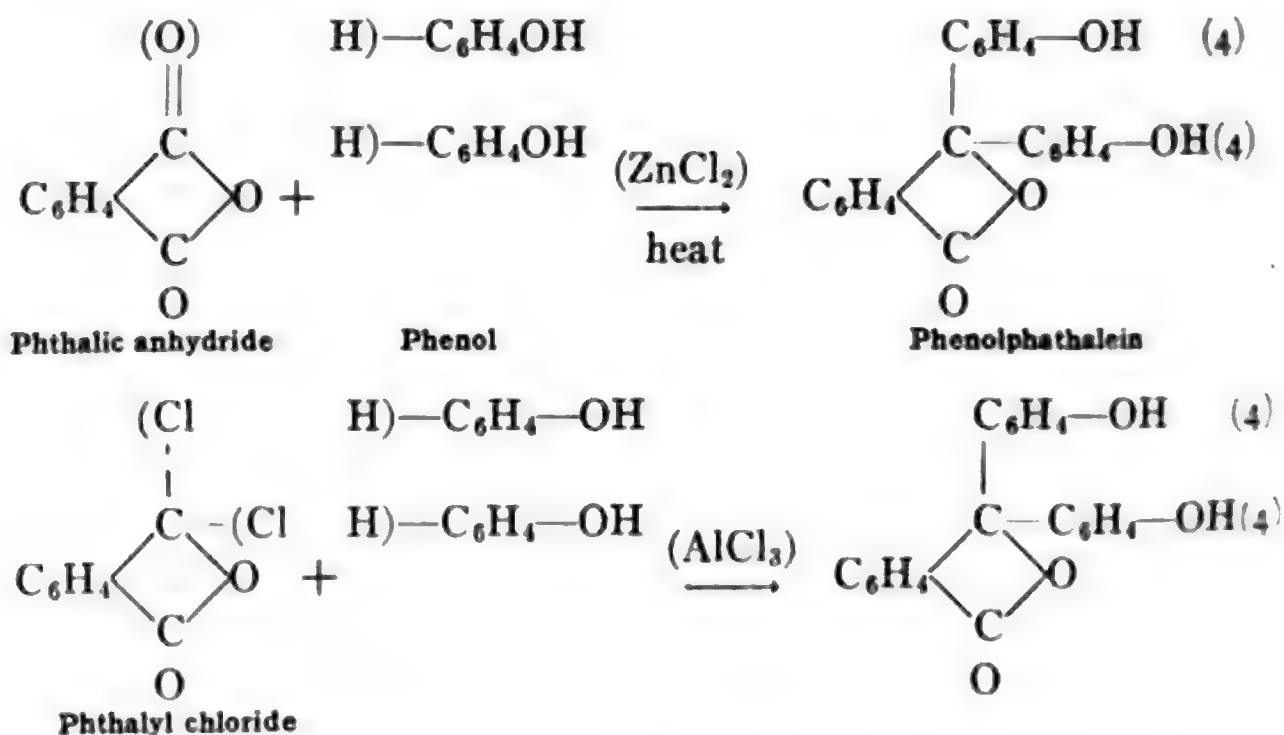
the constitution of the rosanilines. It was first prepared by Runge in 1834 being one of the very oldest dye compounds.

PHTHALEIN DYES

Phenolphthalein

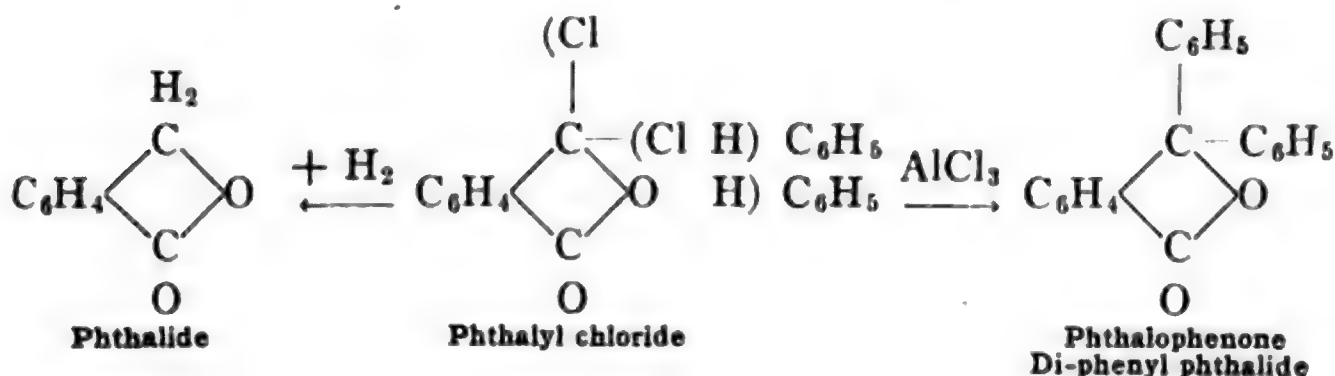
An important group of dyes known as the **phthaleins** and typified by the common indicator **phenolphthalein** are derivatives of tri-phenyl methane, but because they do not possess the same structure as the three preceding groups are placed in a separate series known as the *pyronines*.

Preparation from Phthalic Acid.—In discussing phthalic acid (p. 691) we spoke of the fact that phthalic anhydride or phthalyl chloride with phenol yields phenolphthalein. The reaction takes place in the presence of anhydrous zinc chloride as a dehydrating agent or in the presence of aluminium chloride (Friedel-Craft). Phthalyl chloride being the unsymmetrical compound (p. 692), the two reactions are represented as follows:

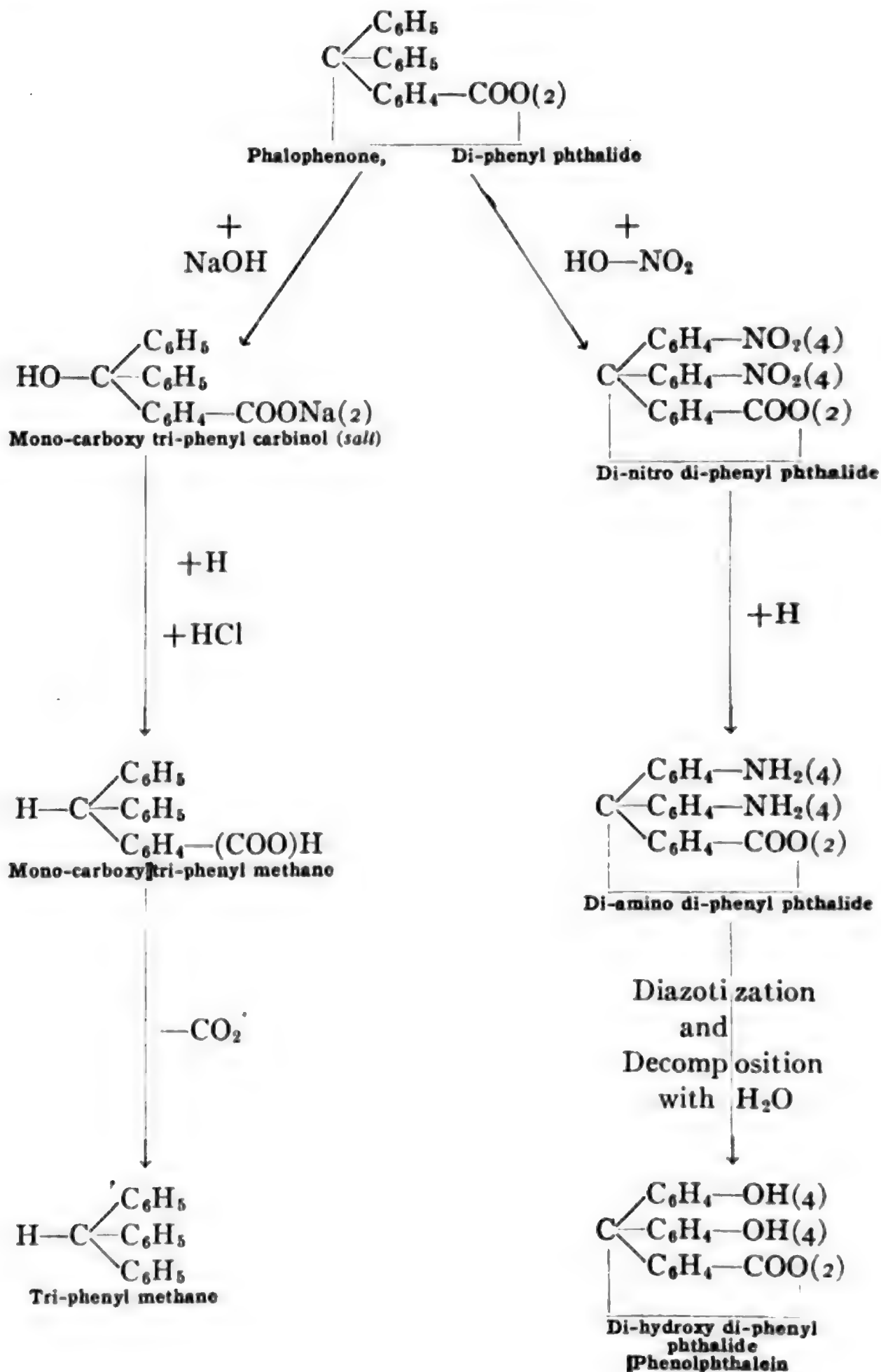


Tri-phenyl Methane Derivative.—That this compound is a derivative of tri-phenyl methane is proven by the following series of relationships. When phthalyl chloride is reduced with hydrogen we obtain **phthalide** (p. 693).

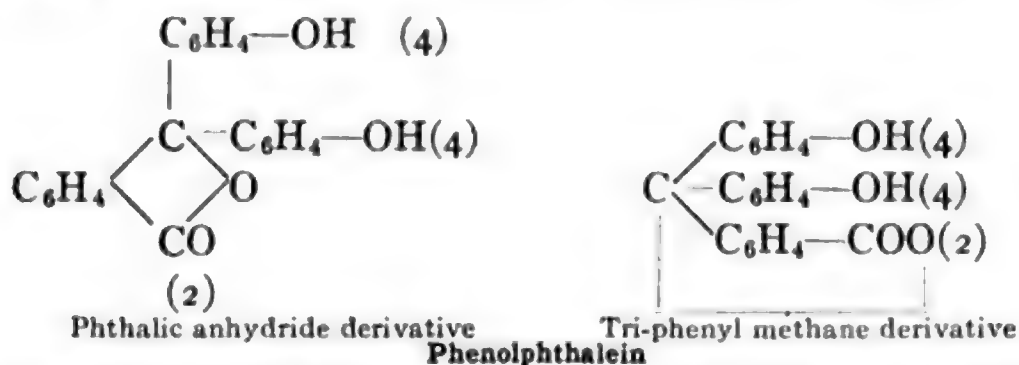
Phthalophenone.—When the chloride is treated with benzene in the presence of aluminium chloride we obtain **phthalophenone** which is **di-phenyl phthalide**, these relationships being



Now when phthalophenone is hydrolyzed with alkalis it yields **mono-carboxy tri-phenyl carbinol** which on reduction yields **mono-carboxy tri-phenyl methane** and this by loss of carbon dioxide yields **tri-phenyl methane**. This means that phthalophenone is a *lactone inner anhydride* of mono-carboxy tri-phenyl carbinol and a true tri-phenyl methane derivative as shown in the reactions below. Now, also, phthalophenone by nitrating yields a di-nitro compound which by reduction yields a di-amino derivative and this by the diazo reaction has the two amino groups replaced by hydroxyls. The result is **phenol phthalein**, which is therefore also a *lactone inner anhydride* of mono-carboxy di-hydroxy tri-phenyl carbinol. All of these relationships may be represented by the following:



The two formulas which we have given for phenolphthalein if compared will be found to be identical.

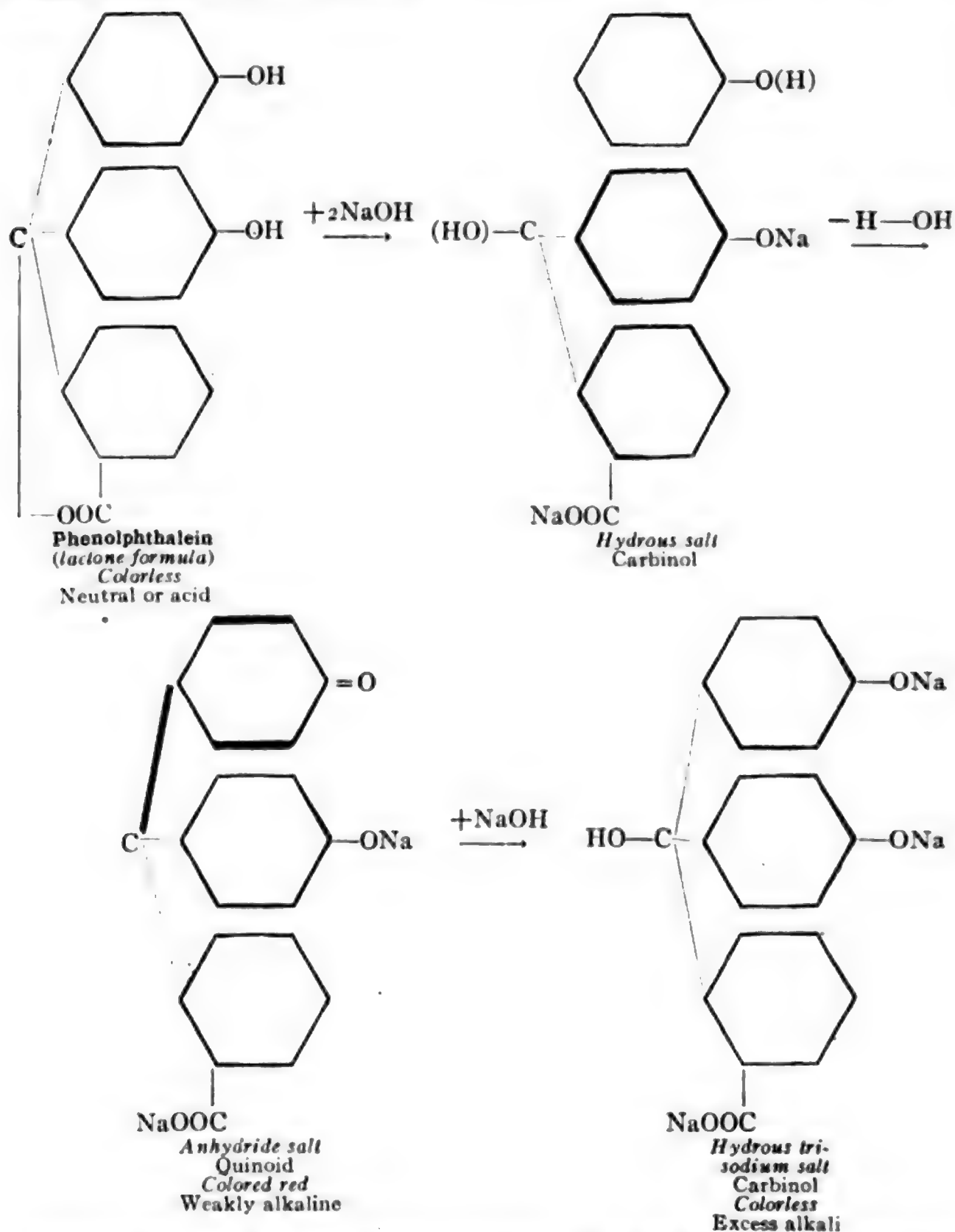


In the first formula the starting point is the benzene ring of phthalic anhydride while in the latter it is one of the carbonyl carbons, the one which in phthalyl chloride is linked to two chlorines.

That a compound formed from phthalic anhydride and phenol should be a derivative of tri-phenyl methane may at first seem strange. If, however, we recall that the preparation of tri-phenyl methane and the rosanilines is from toluene, or its derivatives, in which the methyl carbon in toluene becomes the aliphatic carbon in tri-phenyl methane, then we will recognize that one of the carbonyl carbons in phthalic anhydride, which has its origin in a methyl group in xylene, may also become a methane carbon in a tri-phenyl methane derivative. In fact from our reaction between phthalic anhydride and phenol this carbonyl carbon, which already has attached to it one benzene ring, has substituted in place of the carbonyl oxygen two more benzene rings thus linking to the original methyl carbon three benzene rings, making a tri-phenyl methane compound.

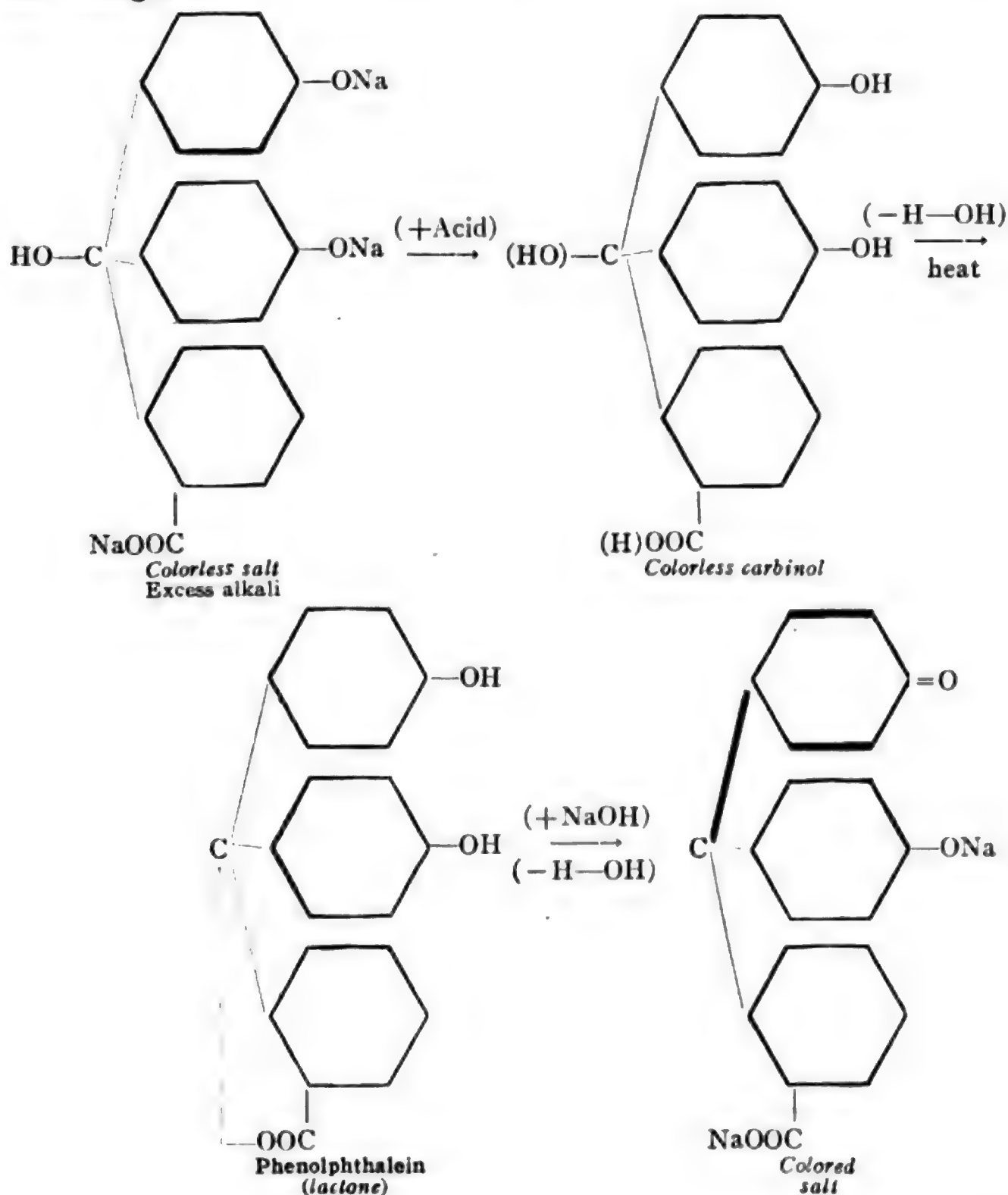
Color and Constitution of Phenolphthalein.—We have used **phenolphthalein** as an example of the *phthalein dyes* in order to show their relation as tri-phenyl methane derivatives. When, however, we attempt to establish a constitution for phenolphthalein which will explain its character as a dye, in harmony with the structure of related compounds, *e.g.*, **fluorescein** and other *pyronine dyes*, we meet with considerable trouble and it may be said that the question is one that does not seem to be cleared up. Strictly speaking phenolphthalein is not a dye. Its well known use as an indicator is associated with the following facts. (1) In *neutral* or *acid* solution it is *colorless*. (2) In *weak alkaline* solution it is *red*. (3) In *strong alkaline* solution it is again *colorless*. (4) On *neutralizing the excess alkali* of (3) with acetic acid and boiling, the *red color is restored* and **phenolphthalein is precipitated**.

Quinoid Structure.—The constitutional relationships of these changes is probably as follows:



When neutral or acid phenolphthalein, a lactone inner anhydride, which is *colorless*, is treated with sodium hydroxide to just alkaline reaction, hydrolysis first takes place yielding the carbinol. This is then neutralized by the alkali yielding a di-sodium salt, one sodium entering the carboxyl group and the other entering one of the phenol

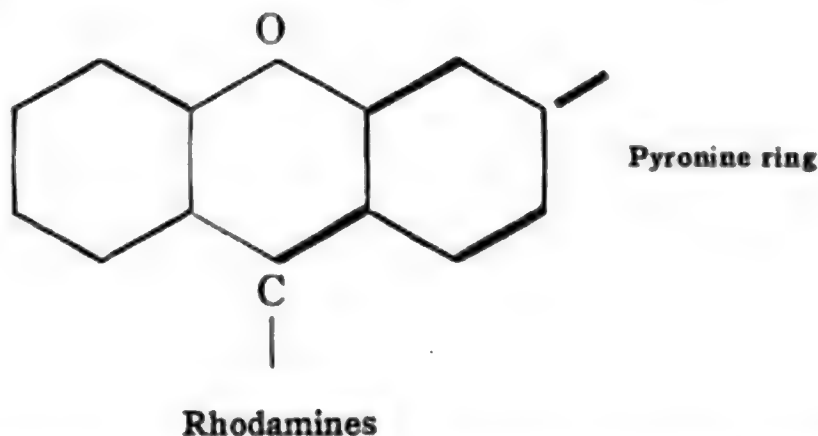
hydroxyls. This salt then loses water from the carbinol and the remaining phenol hydroxyl. This anhydride has the *quinoid* structure and is *colored*. If an excess alkali is added, then hydrolysis and neutralization again take place yielding a tri-sodium carbinol salt, which is *colorless*. If this colorless salt is neutralized with acetic acid the colorless carbinol is first formed which on heating loses water yielding the lactone which is the original phenolphthalein and which is precipitated. In this hydrolysis, however, sodium hydroxide is set free which reacts on the reformed phenolphthalein giving the colored salt again. These last changes are:



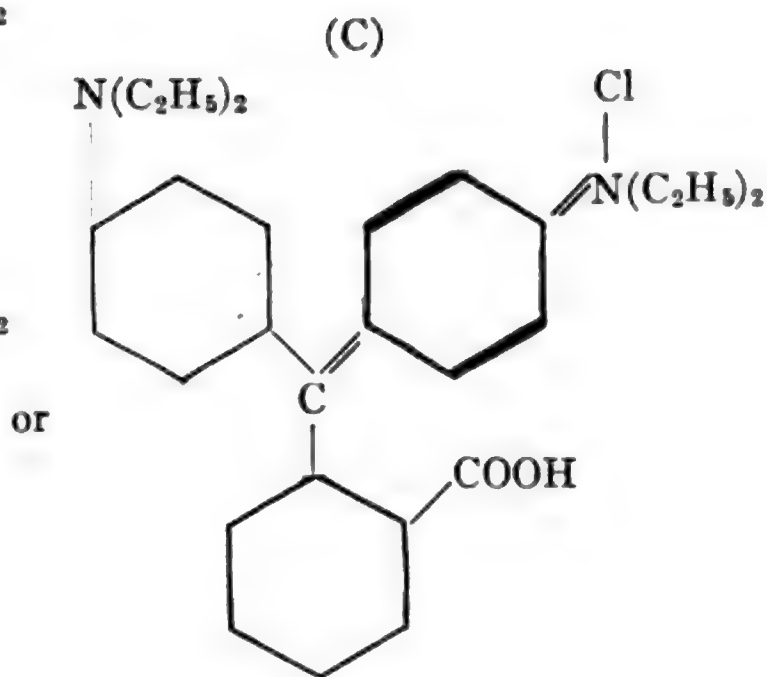
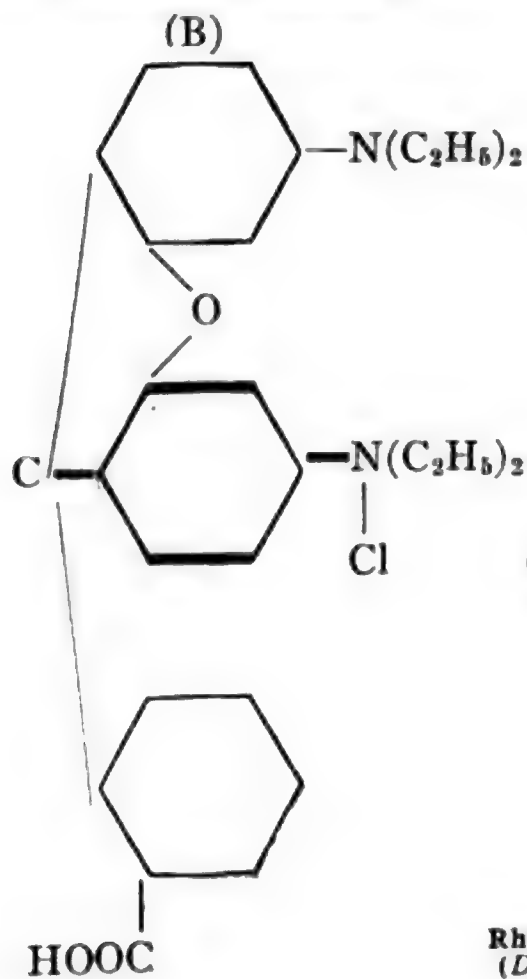
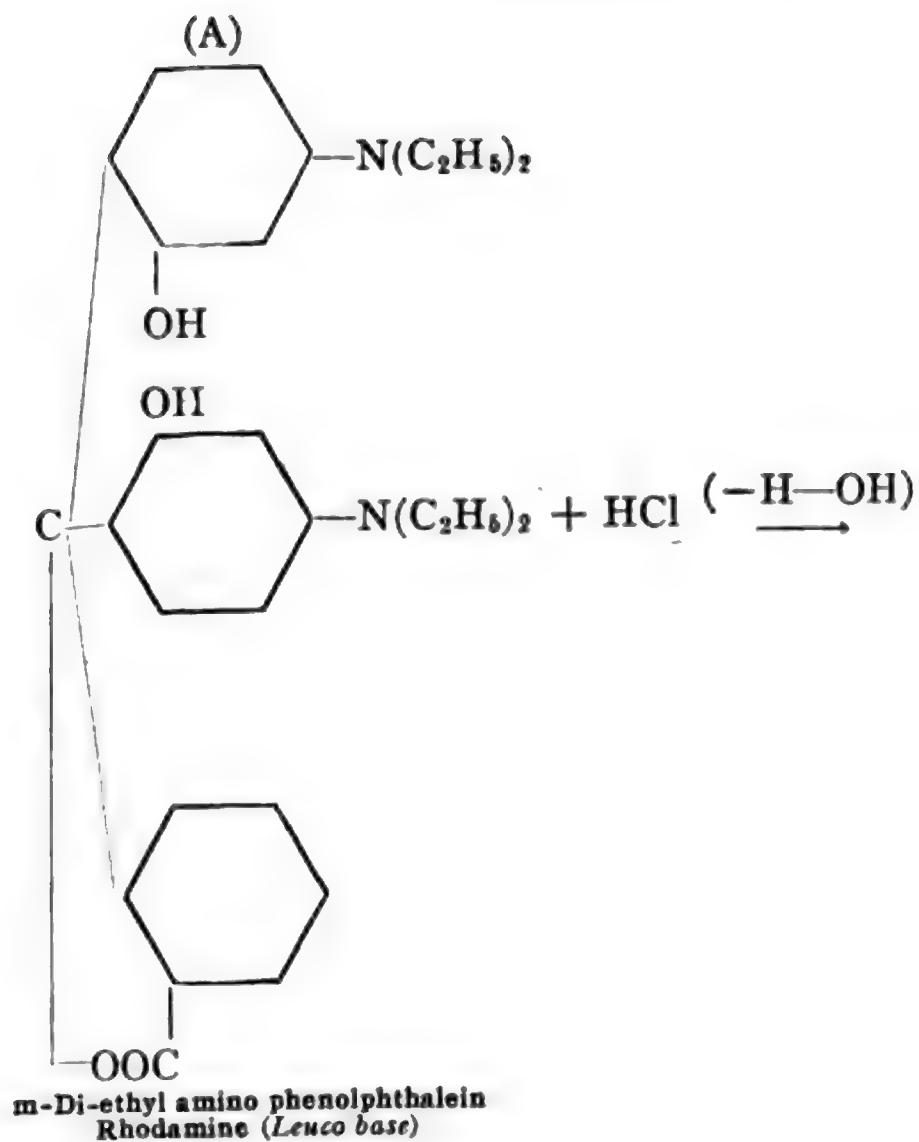
Thus according to this view the change in color of phenolphthalein is due to a change in structure from that of a *lactone* to that of a compound containing a *quinoid ring*. While this quinoid structure is like that which has been established for the colored dye salts of the tri-phenyl methane dyes it has not been directly proven in the case of phenolphthalein. A related phthalein made from **hydroquinol** has been explained by a quinoid structure in which *tetra-valent* or *oxonium* oxygens are present and also by a modified quinoid ring together with the existence of a tautomeric compound. Thus, as previously stated, the exact constitution of phenolphthalein as a color compound is not fully established.

Dissociation Theory.—According to **Ostwald** the color changes in phenolphthalein are explained as due to electrolytic dissociation, the negative *ion* of the salt being colored. In the phenolphthalein itself no dissociation occurs and the compound is thus colorless in neutral or acid solutions. When a salt is formed dissociation takes place and the colored *ions* produce a colored solution. This does not seem quite satisfactory in the case of the tri-sodium salt (p. 754) which evidently does not dissociate as the solution is colorless. This point is explained by the effect of the excess of alkali in retarding dissociation.

Pyronine Structure.—A study of related phthaleins has brought out a structure which apparently applies to all the dyes of this group though here also in the case of phenolphthalein the condition does not wholly fit. We have said that the *phthalein dyes* belong to the group known as *pyronines*. The pyronine ring, which is present in these compounds, has the structure

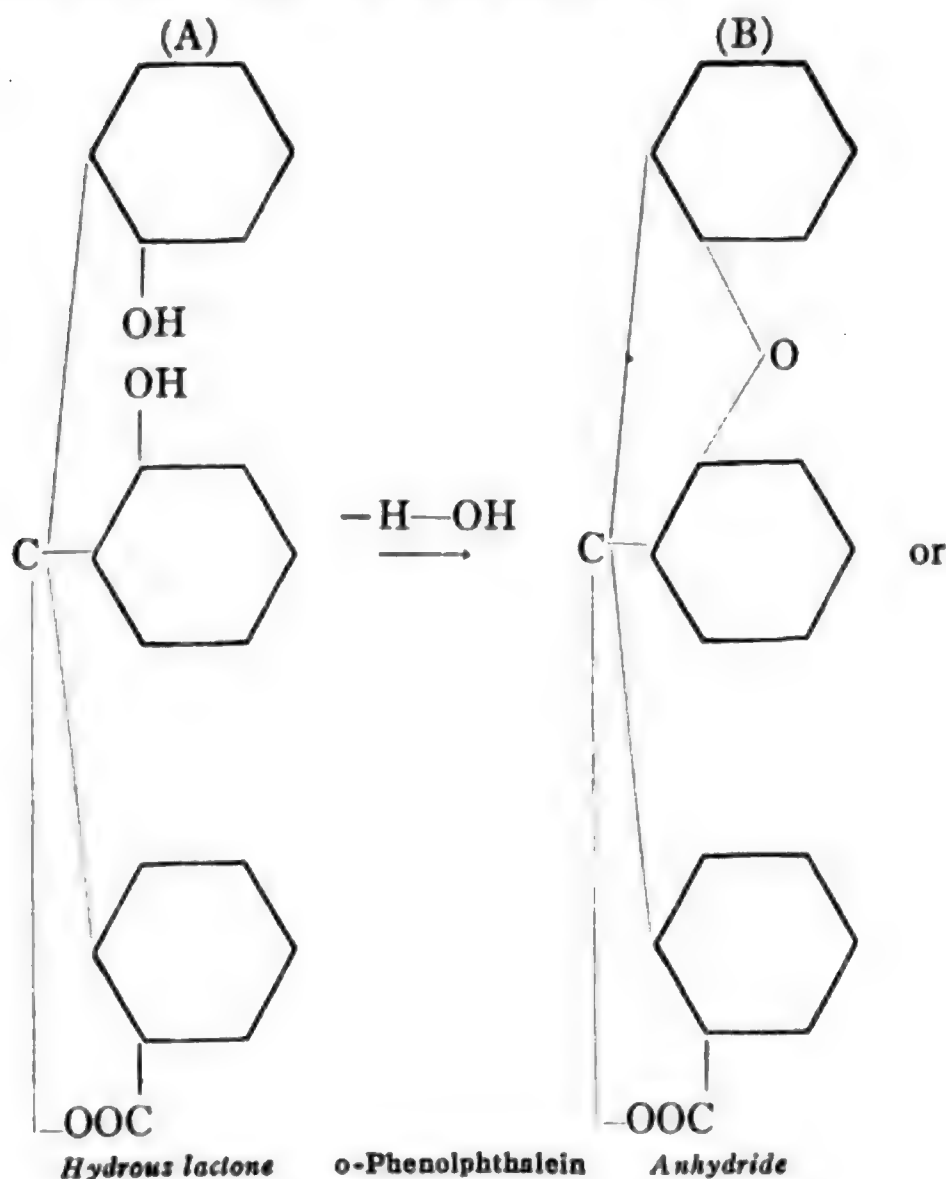


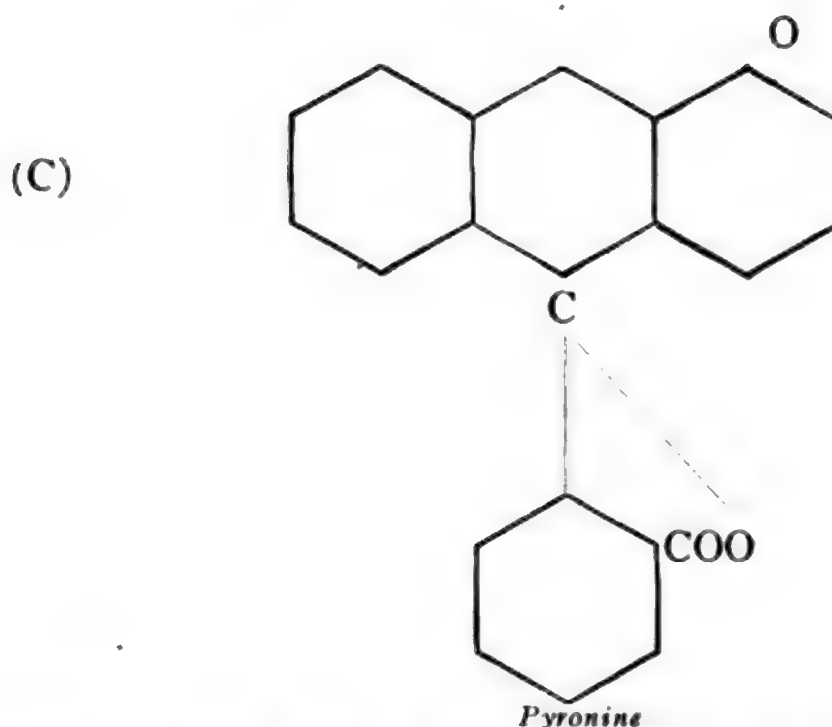
When a phthalein is prepared from phthalic anhydride and **m-di-ethyl amino phenol** the product known as *rhodamine* has the structure of a tri-phenyl methane derivative as follows:



Rhodamine
(Dye Salt)

The leuco base of the rhodamine, (A), is converted into the salt by means of acids, water is lost from the two neighboring phenol groups yielding an anhydride linkage of two of the benzene rings and the lactone form of the base is converted into a quinoid structure in the salt (B). If we write the formula for this salt in a new way but expressing exactly the same structure as by the tri-phenyl methane formula (B), we have formula (C), which contains the *pyronine ring* as given above. Now referring back to the preparation of **phenolphthalein** from **phthalophenone** (p. 752), through the nitro and amino compounds, we see that the relationship is expressed through the *para*-nitro product only. However, in nitrating phthalophenone we are nitrating a benzene compound in which the rings are already linked to a residual methyl carbon. When a methyl group is in the ring nitration effects both the positions *ortho* and *para* to this methyl group. It is found in fact that the *ortho*-nitro derivative is also present, and if we use this *ortho* derivative we obtain finally an **ortho phenolphthalein** the structure of which will be as in (A) below.

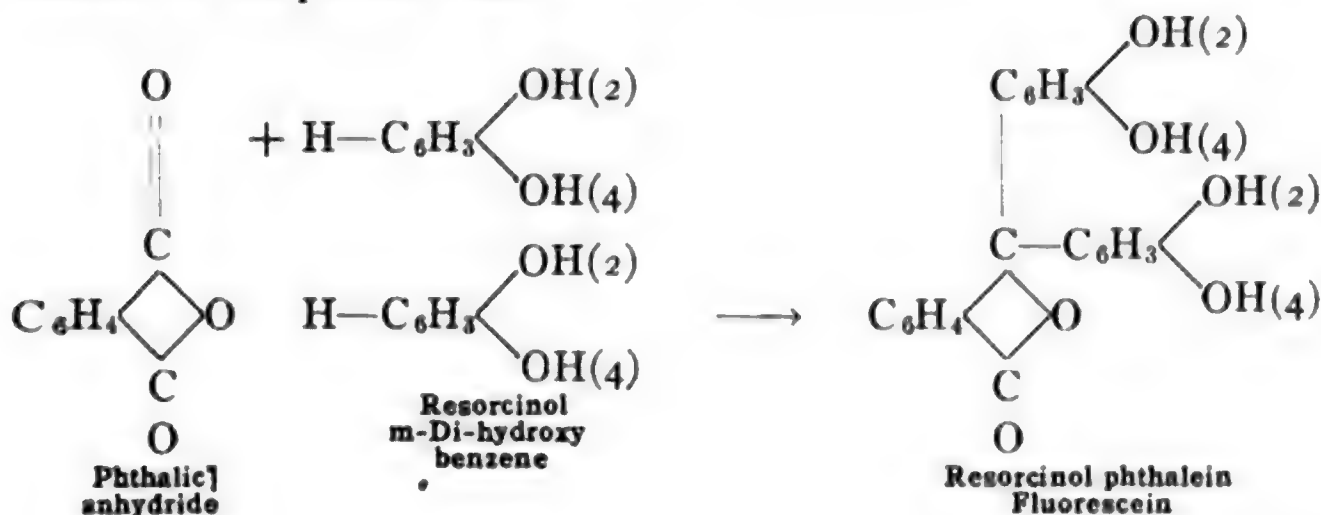


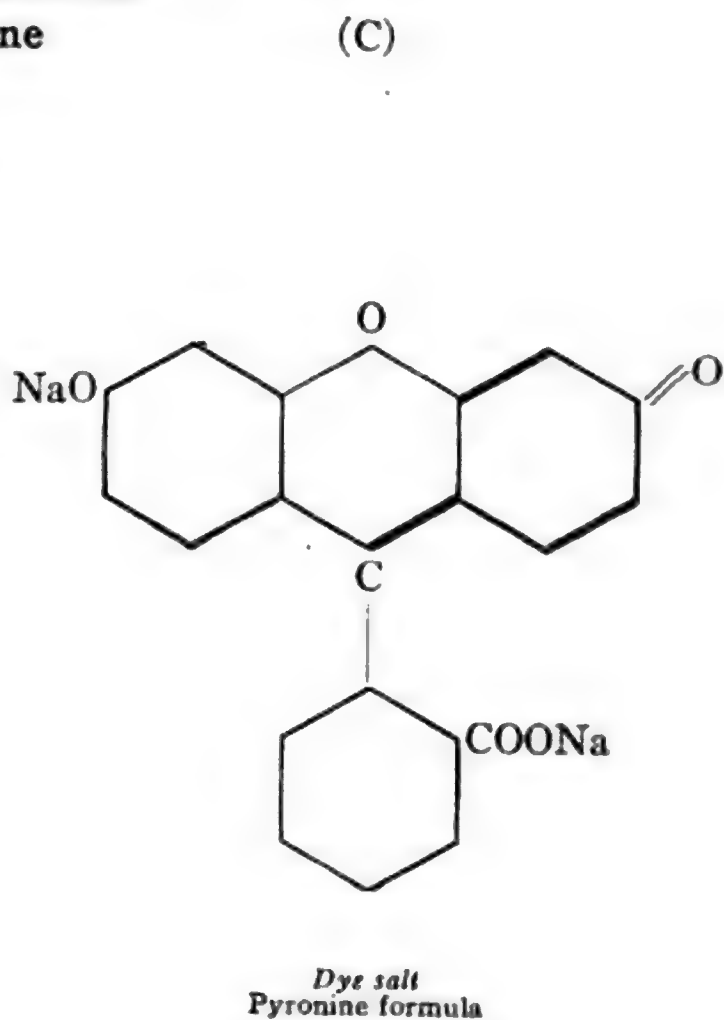
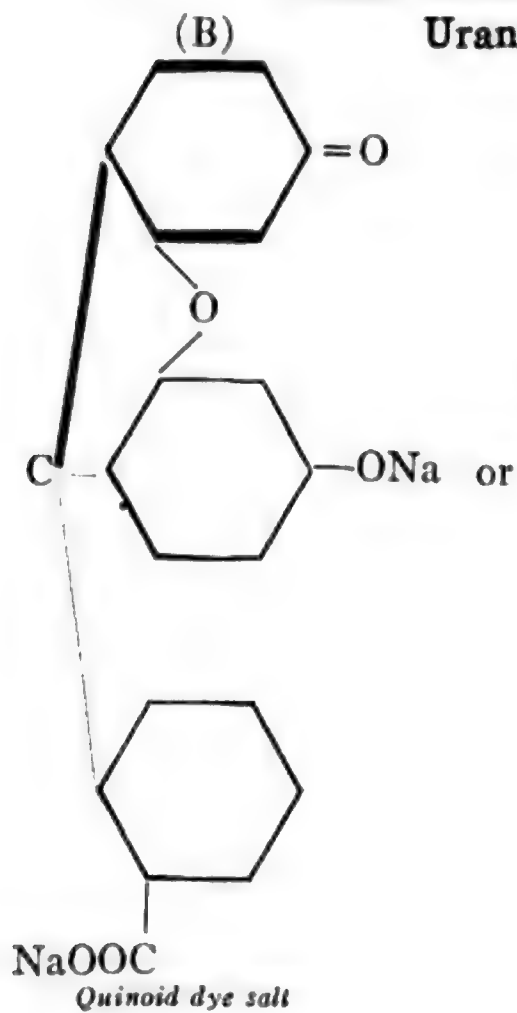
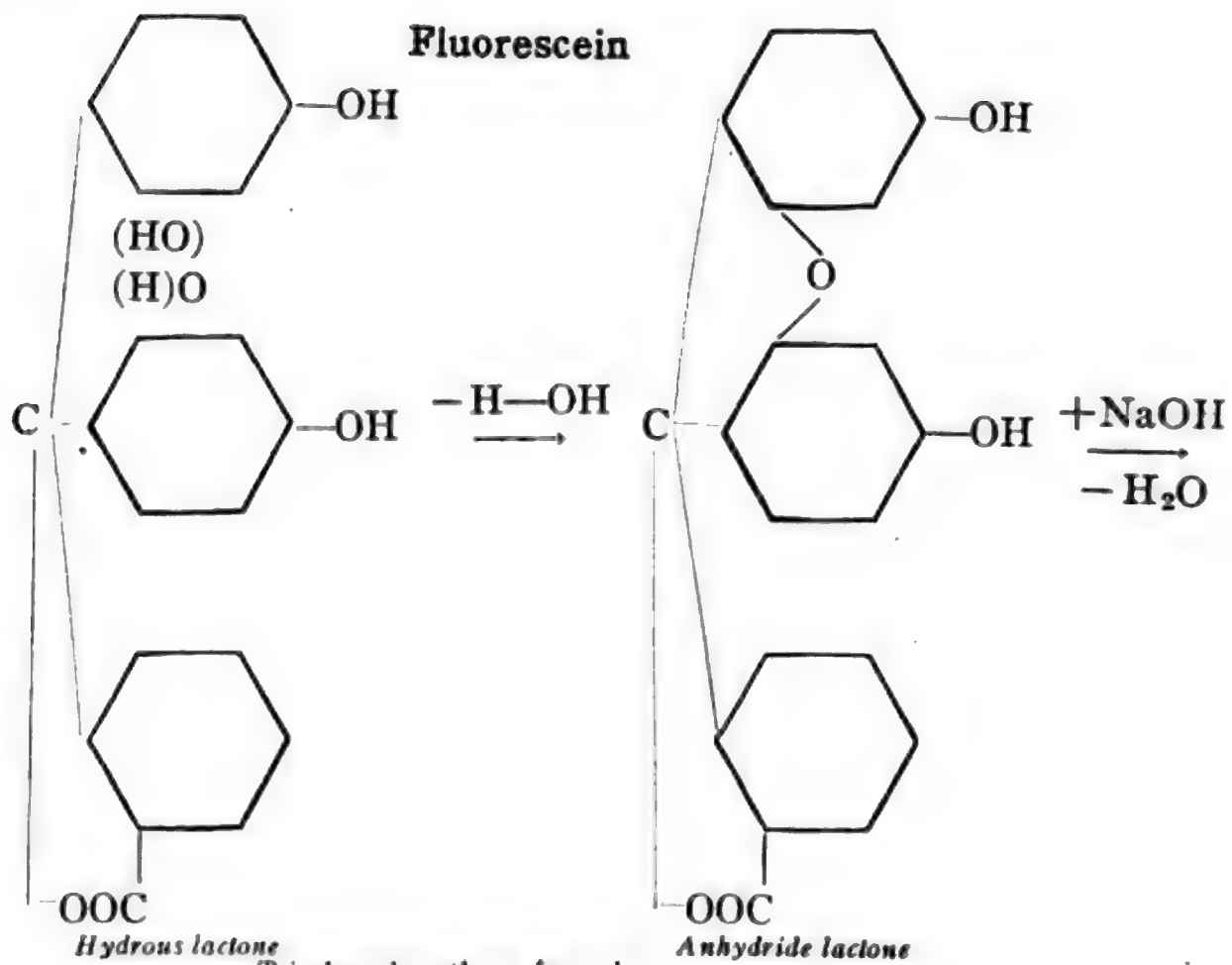


The **o-phenolphthalein** of the lactone formula with two phenol hydroxyls near to each other would lose water and the resulting anhydride if written as in (C) is plainly a *pyronine* as well as tri-phenyl methane derivative as in (B). In this pyronine structure, however, there is no quinoid group and to form such a structure by the conversion of the phenolphthalein into the sodium salt does not appear possible.

Fluorescein

In a related phthalein dye, however, this condition is fully met. The dye fluorescein is **resorcinol phthalein** and is made from **phthalic anhydride** or **phthalyl chloride** and **resorcinol** just as phenol phthalein is made from phthalic anhydride and phenol (p. 750). These relationships may be expressed as follows writing the final dye salt both as a tri-phenyl methane derivative (B) and as a pyronine (C). The reactions are exactly analogous to those given for the preparation of phenolphthalein and its *dye salt* (p. 750), some of the intermediate steps being omitted in the present case.

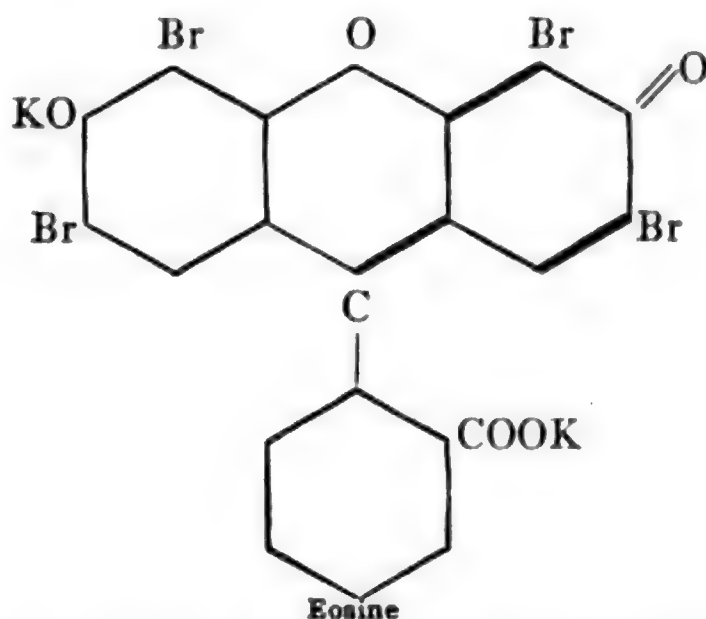




Uranine.—Phenolphthalein is a yellow crystalline compound, m.p. 250° . It is practically insoluble in water but is readily soluble in alcohol in which form it is used as an indicator. Fluorescein is a dark red crystalline compound, practically insoluble in water but soluble in alcohol. Its sodium salt is red in color but in dilute solution exhibits a remarkable green and yellow fluorescence, hence the name **fluorescein**. The salt is known as **uranine**. It is not used as a dye by itself because of its faint character but is used to mix with others in order to impart fluorescence. The rhodamines also possess fluorescent properties mostly blue and red.

Eosine

A derivative of fluorescein is important as a dye. It is known as **eosine** from the Greek word for *dawn* because its color is a fluorescent rose like the color of the sky at dawn. It is used as a silk dye. It is the *tetra-bromine* derivative of fluorescein potassium salt.



The preceding discussion of the tri-phenyl methane and pyronine dyes is by no means exhaustive but enough has been said to give the student some idea of the importance of the dye compounds which are derived from the hydrocarbon **tri-phenyl methane**; also to give the principal facts in connection with their relation to the history of synthetic dyes and to the question of chemical constitution and color of dyestuffs.

This discussion of the constitution of phenolphthalein and fluorescein involves the work of numerous investigators. Among these we

may mention the following: von Baeyer, Bernthsen, Friedlander, Herzig, R. Meyer, O. Fischer, Green and Perkin, Acree, Ostwald.

Tri-phenyl Methyl

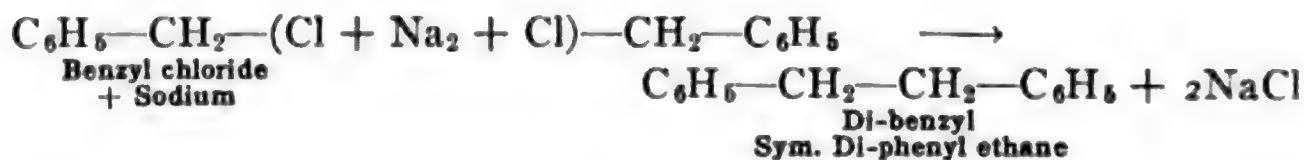
Before leaving the general subject of tri-phenyl methane mention should be made of a compound recently discovered and investigated principally by **Gomberg**. This compound is **tri-phenyl methyl** $(C_6H_5)_3\equiv C$. The importance of the compound is that it is a case of a compound containing a *tri-valent carbon atom*. In other words it is a derivative of the free radical methyl (CH_3) . A discussion of this compound in any detail would involve many new ideas, especially concerning the existence of compounds in equilibrium with each other; and as such a study is beyond the province of this text it will not be entered into. We may simply add that on account of the importance of his investigations on this compound and the general question of tri-valent carbon **Gomberg** was awarded the **Nichols medal** in 1914.

Di-benzyl, Stilbene, Tolane

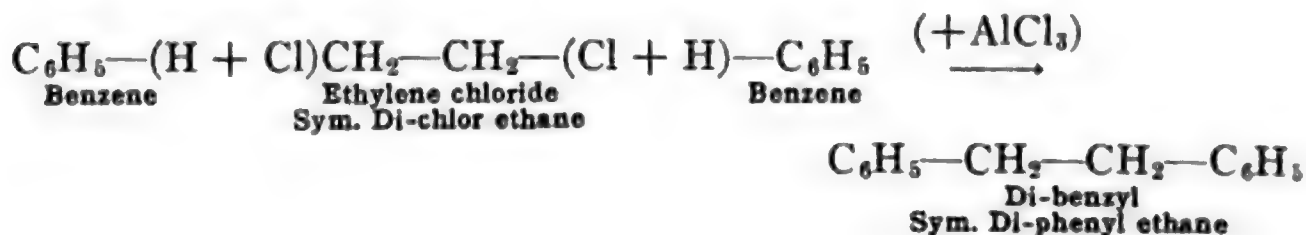
In making di-phenyl methane benzyl chloride reacts with phenyl chloride in the presence of sodium.



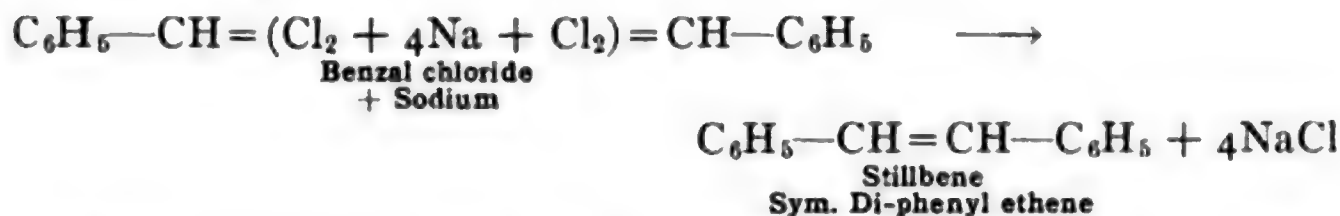
When, however, benzyl chloride alone is treated with sodium we obtain a compound known as di-benzyl.



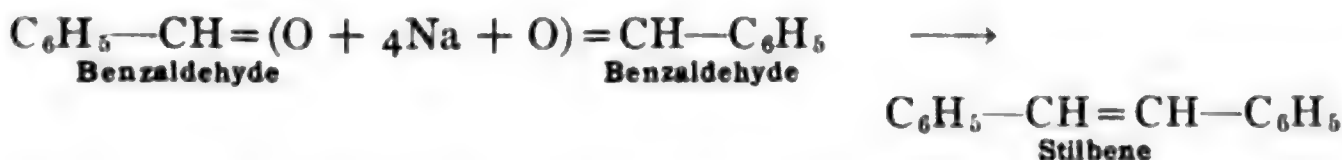
Di-benzyl is therefore symmetrical di-phenyl ethane as is also proven by its preparation from symmetrical di-chlor ethane, by the **Friedel-Craft reaction**, with benzene as follows:



The reaction of benzyl chloride with sodium also takes place with **benzal chloride** and sodium yielding an ethylene unsaturated compound corresponding to di-benzyl.



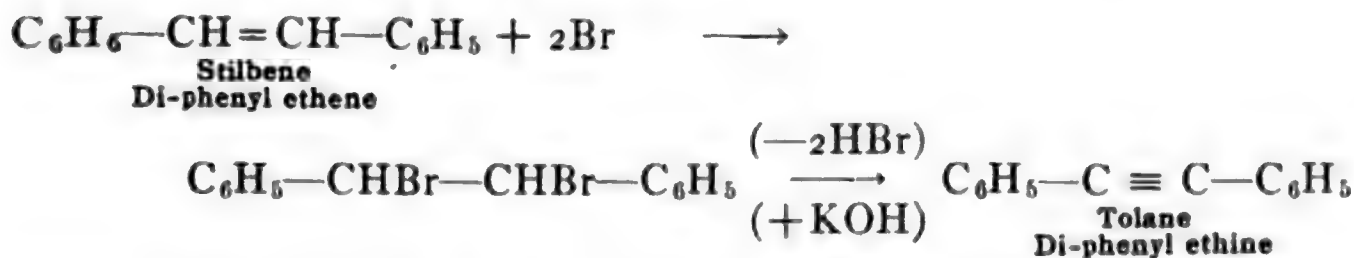
This compound which is **sym. di-phenyl ethene** is known as **stilbene**. Two other syntheses of stilbene are interesting. When **benzaldehyde** is distilled over sodium two molecules lose oxygen and the benzal radicals unite.



Also when the vapor of **toluene** is passed over heated lead oxide stilbene



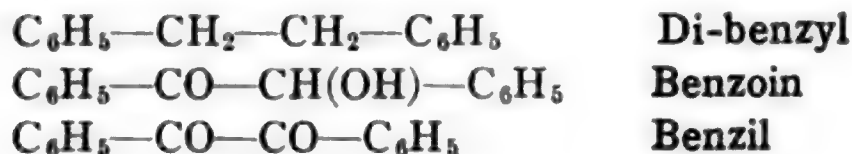
results. From stilbene by means of the addition of bromine and subsequent loss of hydrogen bromide, by treatment with alcoholic potassium hydroxide the corresponding acetylene *triple bond* compound is obtained. This is known as **tolane**.



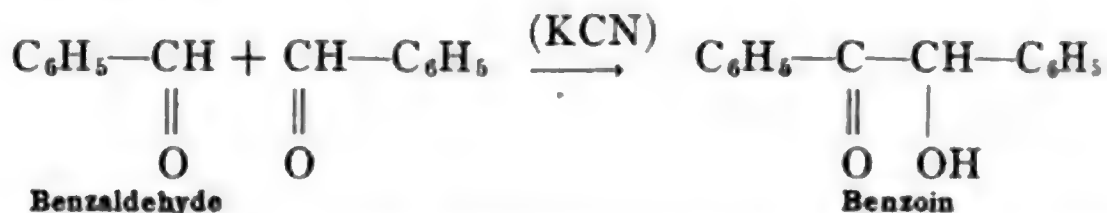
Stilbene is important in connection with the constitution of **phenanthrene** (p. 807) and amino derivatives of stilbene yield dyes.

Benzoin. Benzil

Two derivatives of di-benzyl should be mentioned, viz., **benzoin** and **benzil**.



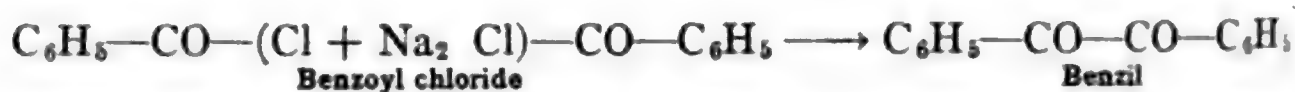
Benzoin is formed by the condensation of **benzaldehyde** with itself when heated with potassium cyanide. This is analogous to the **aldol condensation** (p. 169).



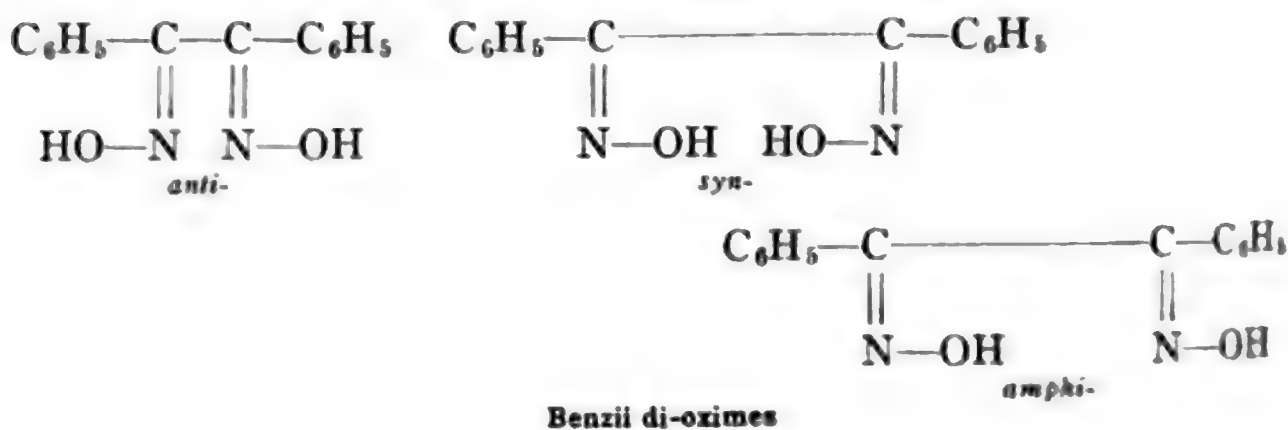
This compound is a mixed *alcohol-ketone* compound. When oxidized with nitric acid or chlorine the alcoholic group is converted into a ketone group and a *de-ketone* known as **benzil** is obtained.



Benzil is also obtained when **benzoyl chloride** is treated with sodium amalgam.



Benzoin being an *alcohol-ketone* similar to carbohydrates yields *osazones*, and both benzoin and benzil as *ketones* yield *oximes*. The *di-oxime* of benzil exists in three stereo-isomeric forms.

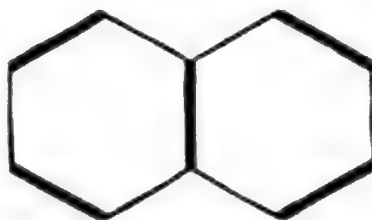


3. CONDENSED RING COMPOUNDS

We come now to a third series of aromatic hydrocarbons, termed *condensed ring compounds*. They are composed, not of a single ring, as are benzene and its homologues, nor of two or more rings linked together, usually with an intervening carbon group, as in di-phenyl and related compounds, but of *two or more rings condensed together*. Just what is meant by this term condensed rings will be understood when we establish the constitution. Three important hydrocarbons of this series are known, viz., **naphthalene**, **anthracene** and **phenanthrene**. All of these three hydrocarbons yield derivatives of the same classes as those derived from benzene and many of them, especially those of the first two hydrocarbons, are of particular importance as dyes. Each hydrocarbon with its derivatives will be considered in turn.

NAPHTHALENE AND DERIVATIVES

Naphthalene, $C_{10}H_8$,



Coal Tar Source.—Naphthalene is the common substance used in place of camphor and known as *moth balls*. It is obtained from coal tar and is present in illuminating gas being often found as a crystalline deposit in the gas mains. It is present in coal tar more abundantly than any other individual compound, the yield being about 6.0–10.0 per cent. Most of the naphthalene is present in the second fraction or *middle oil* obtained from the first fractional distillation of coal tar, i.e., the fraction distilling between 170° – 230° . This is redistilled and the crude naphthalene is collected in large cooling tanks where it forms a beautiful crystalline deposit. The adhering oil is removed by means of a heated hydraulic press and the thus partially purified product is treated with acids and alkalies and again distilled through a rectifying still. The product so obtained is about 90–95 per cent pure and may be still further purified by sublimation. Naphthalene when pure crystal-

lizes in shining flakes, m.p. 79.6° , b.p. 218° . It is insoluble in water but distils with steam. It sublimes when heated and volatilizes even at ordinary temperatures. It is soluble in ether and in hot alcohol.

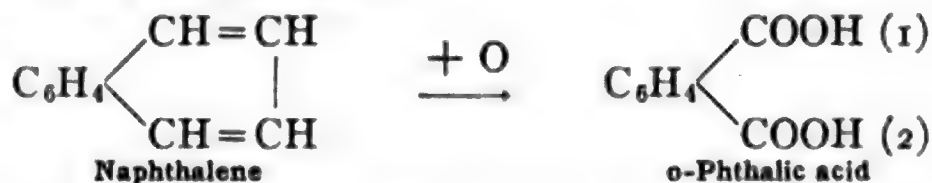
Naphthalene as such has several important uses. Its most common use is as a germicide or insecticide against the attacks of the moth miller larvæ in the form of what is known as moth-balls. A more important use is as an enricher or carburetter of water gas for illuminating purposes. As it contains a large amount of carbon it burns with a very luminous flame and thus makes more luminous a weakly illuminating gas. The most important uses of all, however, are as a source of **ortho-phthalic acid** and in yielding derivatives which are used as dyes.

The commercial method of preparing *ortho*-phthalic acid is from naphthalene and the cheapness of this process has been essential, as we have previously stated, to the commercial synthesis of **indigo** (p. 880). The method originally used was to convert naphthalene into its *tetrachloride* and then oxidize this (p. 771). Recently the process consists in the oxidation of naphthalene with fuming sulphuric acid in presence of mercury salts or salts of rare earths which act as catalyzers. The oxidation takes place with the oxygen of the air, the mercury and sulphuric acid being entirely recovered. An electrolytic process by which naphthalene becomes oxidized to **phthalic acid** and **naphthoquinone** has also been used. The reactions of these processes so far as the naphthalene is concerned will be discussed now in connection with the study of its constitution. An indirect process for converting naphthalene into phthalic acid is through the hydroxyl derivatives or *naphthols* (p. 783), by fusion with potassium hydroxide in presence of metal oxides.

Constitution.—The composition of naphthalene is represented by the formula $C_{10}H_8$. What is its constitution? In the first place it is a hydrocarbon *similar* in its chemical properties to **benzene** and not to methane. It readily forms nitro and sulphonic acid derivatives and its hydroxyl derivatives are *analogous to phenols*, not to alcohols. It also yields hydrogen and halogen addition products like benzene. The true constitution of the compound has been established by reactions both of decomposition and of synthesis.

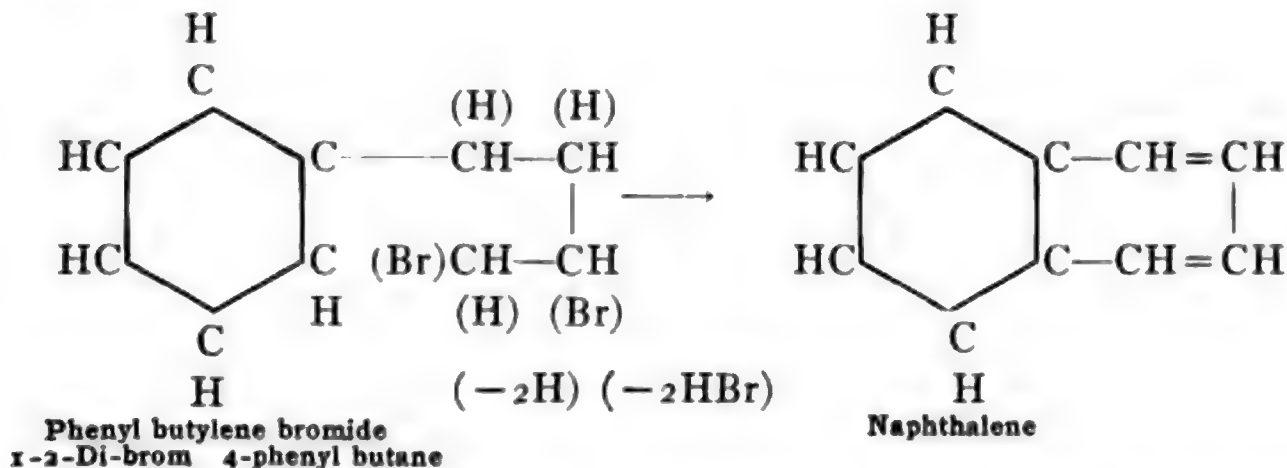
Yields ortho-Phthalic Acid.—The simplest proof that naphthalene does contain a *benzene ring* is found in the fact that on oxidation it yields **phthalic acid** and *always* the *ortho* compound. This would indicate

that in naphthalene there must be present a benzene ring with side chain carbon groups linked to it in two positions *ortho* to each other. If, in the empirical formula $C_{10}H_8$, we allow for a di-substituted benzene ring, *i.e.*, C_6H_4 , we shall have left a group, C_4H_4 , and the formula for naphthalene may be written $C_6H_4 = C_4H_4$. As the group C_4H_4 is linked to the ring in two positions the simplest and practically the only way in which we may consider it is as four CH groups linked together so as to satisfy the tetra-valence of carbon. The formula and above reaction may then be represented.



The easy oxidation of such unsaturated side chains would be expected (p. 670).

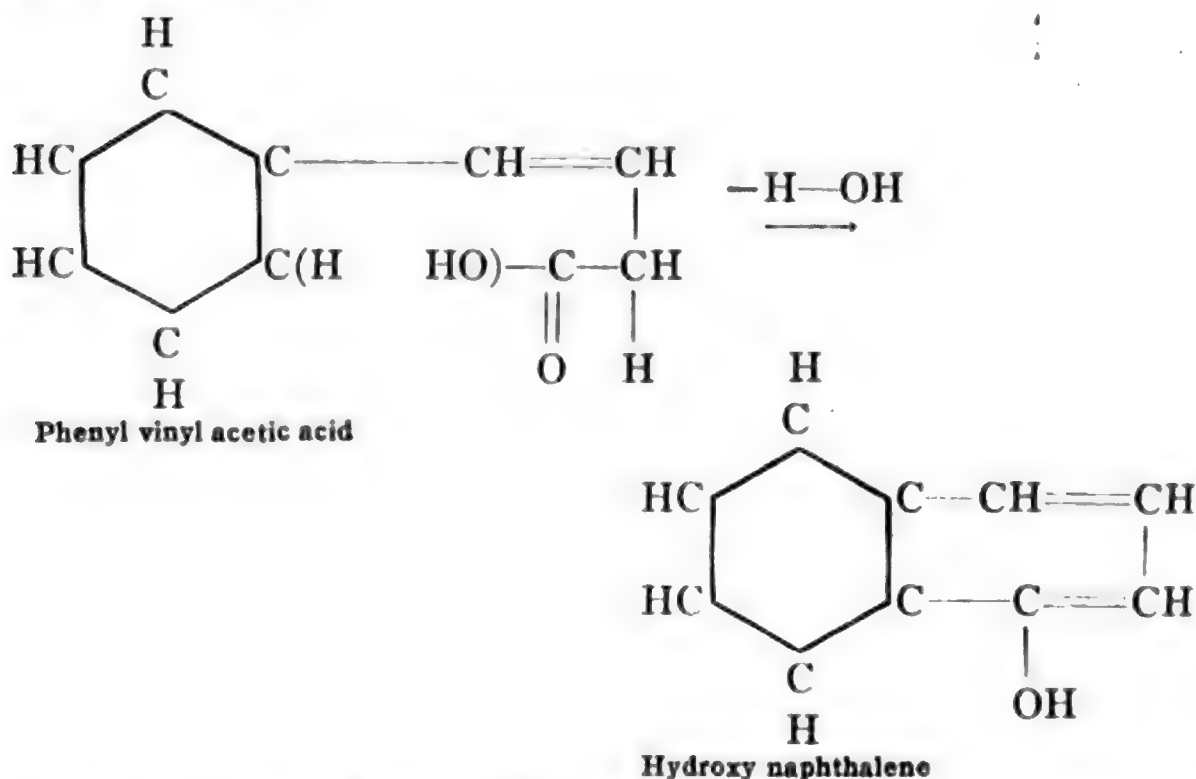
Synthesis from Phenyl Butylene Bromide.—That this must represent the constitution, at least in part, is proven by the synthesis of naphthalene from **phenyl butylene bromide**. When **4-phenyl Δ_1 -butene**, *i.e.*, $C_6H_5-CH_2-CH_2-CH=CH_2$ (p. 158), is treated with bromine two atoms of the halogen add on to the double linked carbons giving **phenyl butylene bromide**, $C_6H_5-CH_2-CH_2-CHBr-CH_2Br$, **1-2-di-brom 4-phenyl butane**. This compound on heating loses two molecules of hydrogen bromide and also two atoms of hydrogen and the product is naphthalene. From what has been previously proven this reaction must result in linking the aliphatic side chain at a second point in the benzene ring *ortho* to the one already held. The reaction is, therefore,



It should be emphasized also that in phenyl butylene bromide we have a space relationship exactly the same as in the case of an *epsilon*-

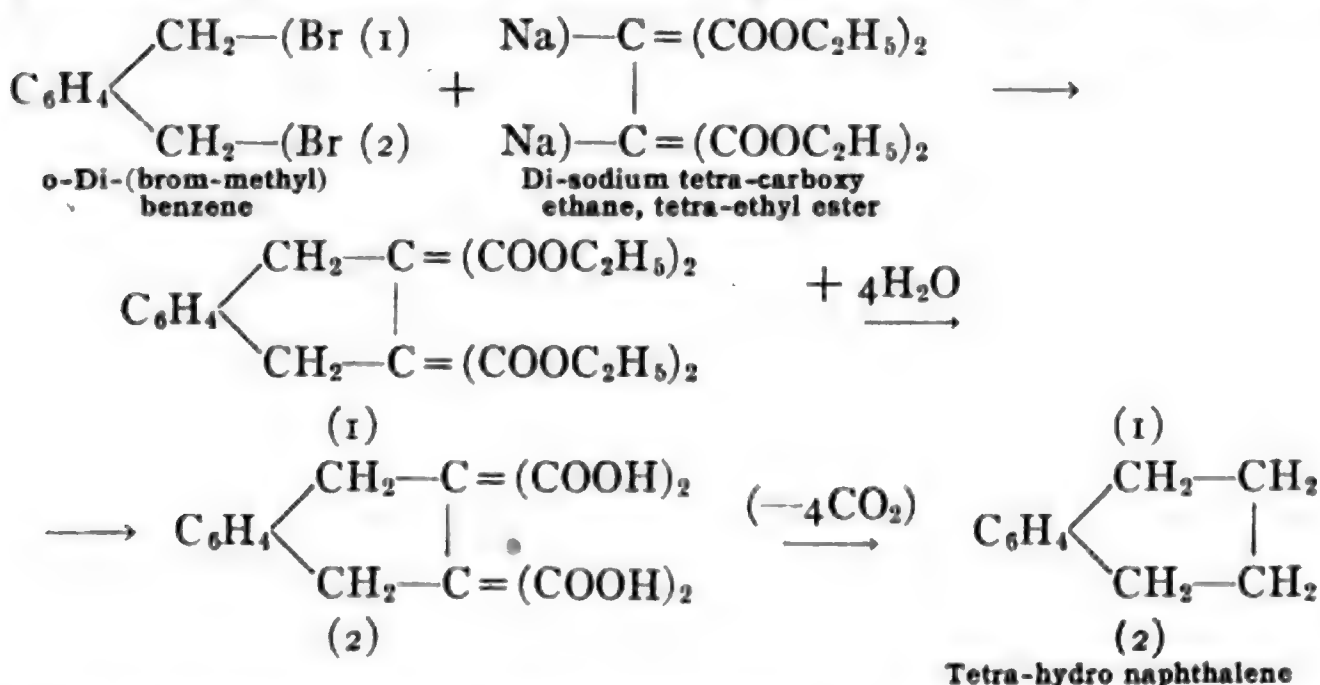
hydroxy acid which, like the *gamma*- and *delta*-acids, readily lose water yielding a lactone anhydride (p. 242). The *ortho* carbon of the ring and the end carbon of the butane side chain are the ends of a six carbon chain so that the bromine linked to one and the hydrogen linked to the other are in very close proximity. Hydrobromic acid, HBr , is therefore easily lost and the *end of the side chain* becomes linked to the *ortho* carbon of the ring. As in similar cases this is clearly seen if tetrahedral models are used.

From Phenyl Vinyl Acetic Acid.—A second synthesis very closely analogous to the preceding is from **phenyl vinyl acetic acid** (p. 700), which has the constitution $\text{C}_6\text{H}_5\text{—CH=CH—CH}_2\text{—COOH}$. When this is heated it loses water and yields a *hydroxy naphthalene* or *naphthol* in which the hydroxyl is linked to the carbon next to the *ortho* carbon of the ring.

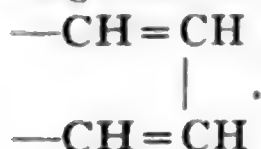


From Tetra-carboxy Ethane.—**1-1-2-2-Tetra-carboxy ethane** which may be prepared as the tetra-ethyl ester by the malonic ester synthesis (p. 276), yields a di-sodium compound analogous to the mono-sodium compound of malonic ester. This compound is $(\text{C}_2\text{H}_5\text{—OOC})_2 = \text{CNa—NaC} = (\text{COOC}_2\text{H}_5)_2$. Now when this compound reacts with *ortho*-di-(brom-methyl) benzene, C_6H_4 , which is made from *ortho*-xylene, two molecules of sodium bromide are

eliminated and after hydrolysis of the resulting ester and loss of four molecules of carbon dioxide from the resulting acid the final product is a *tetra-hydrogen addition product* of **naphthalene**. The reactions are,

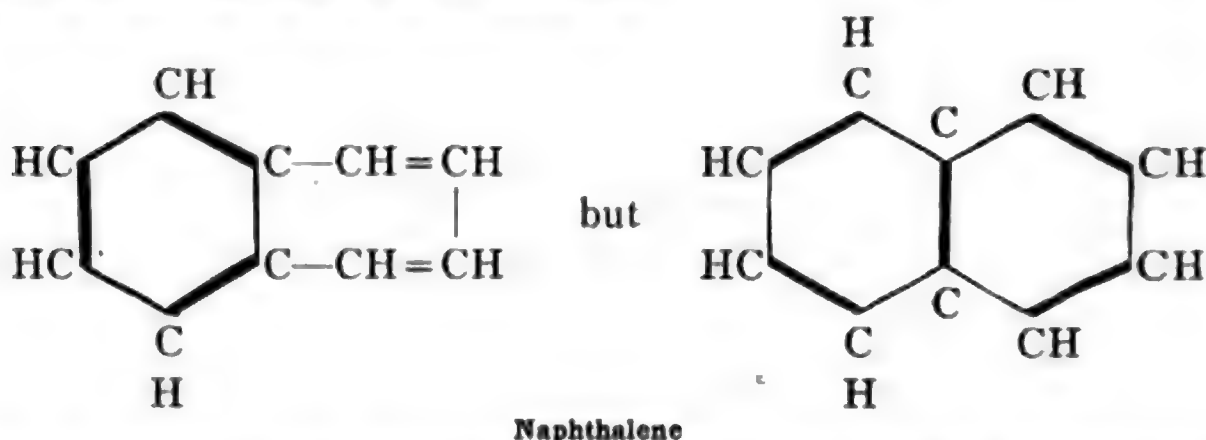


Thus the constitution of naphthalene must be represented as a benzene ring linked in two positions ortho to each other to the unsaturated group,

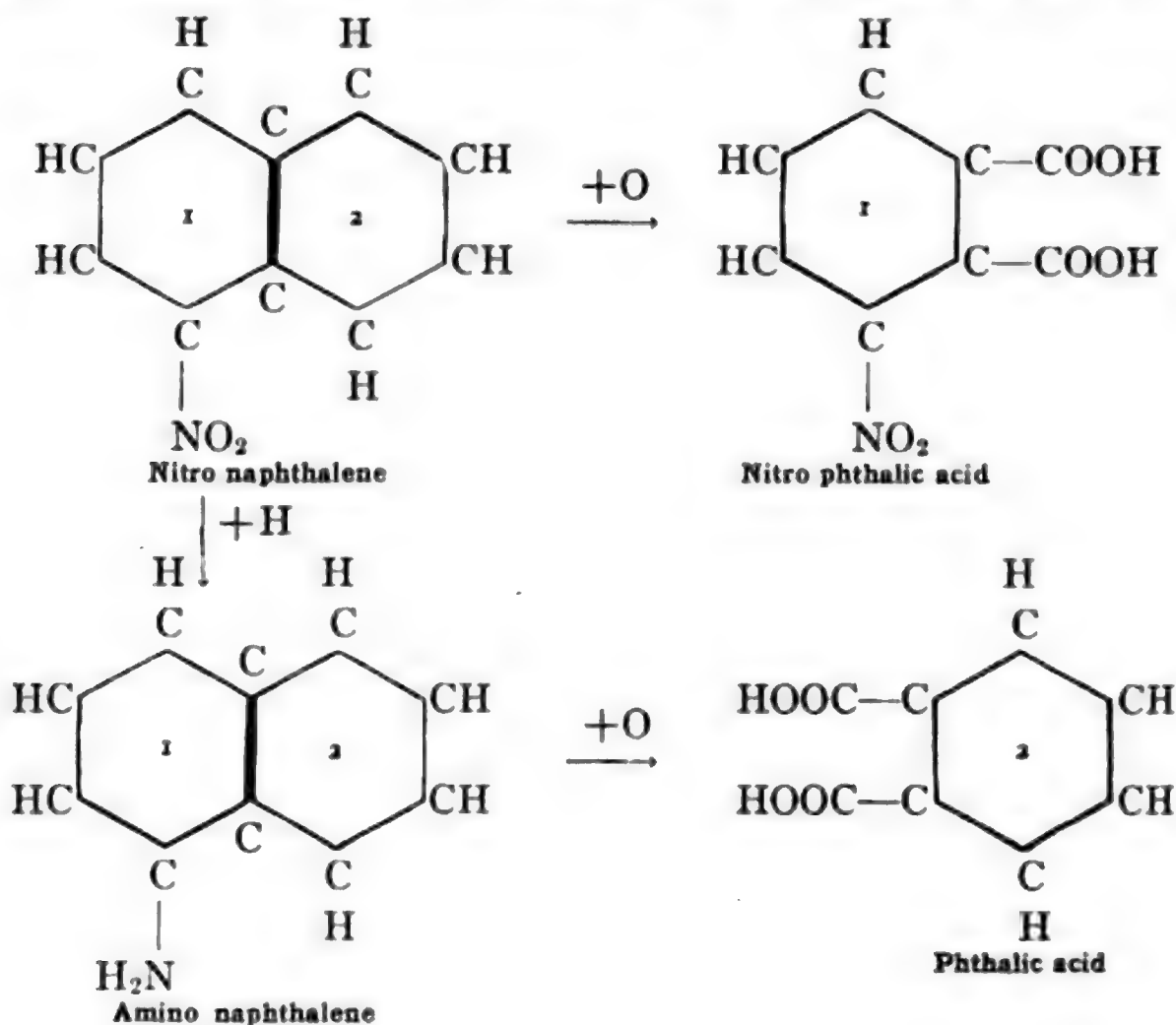


Two Benzene Rings. Erlenmeyer. Graebe.—The work of Graebe on the oxidation products of **nitro naphthalene** and **amino naphthalene** throws yet more light upon this constitution and sustains an idea first suggested by **Erlenmeyer** that naphthalene contains not one benzene ring only but *two such rings condensed together*. We have said that naphthalene on oxidation yields phthalic acid. Now by substituting a nitro group in naphthalene **nitro naphthalene** is obtained. This nitro naphthalene is easily reduced to **amino naphthalene** with the amino group evidently occupying the *same position* as the nitro group. Now it is a striking fact that on oxidation the **nitro naphthalene** yields **nitro ortho-phthalic acid** but the **amino naphthalene** yields **ortho-phthalic acid**, without any substituting group in the benzene ring other than the carboxyls. In one case the nucleus of naphthalene which contains the nitro group remains *as a benzene ring* in nitro phthalic acid while in the other case the nucleus of naphthalene which contains the amino group, which must be the *benzene ring* of nitro naphthalene and nitro phthalic acid, is *destroyed*, yet there *remains* an unsubstituted

benzene ring in the phthalic acid. Therefore in naphthalene there must be *two benzene rings*, or better, two parts either one of which remains as a benzene ring on the oxidation of the other part to two carboxyls. If the formula for naphthalene as we have written it be built up of tetra-hedral models we shall find that the two halves are exactly alike and our formula should be written not

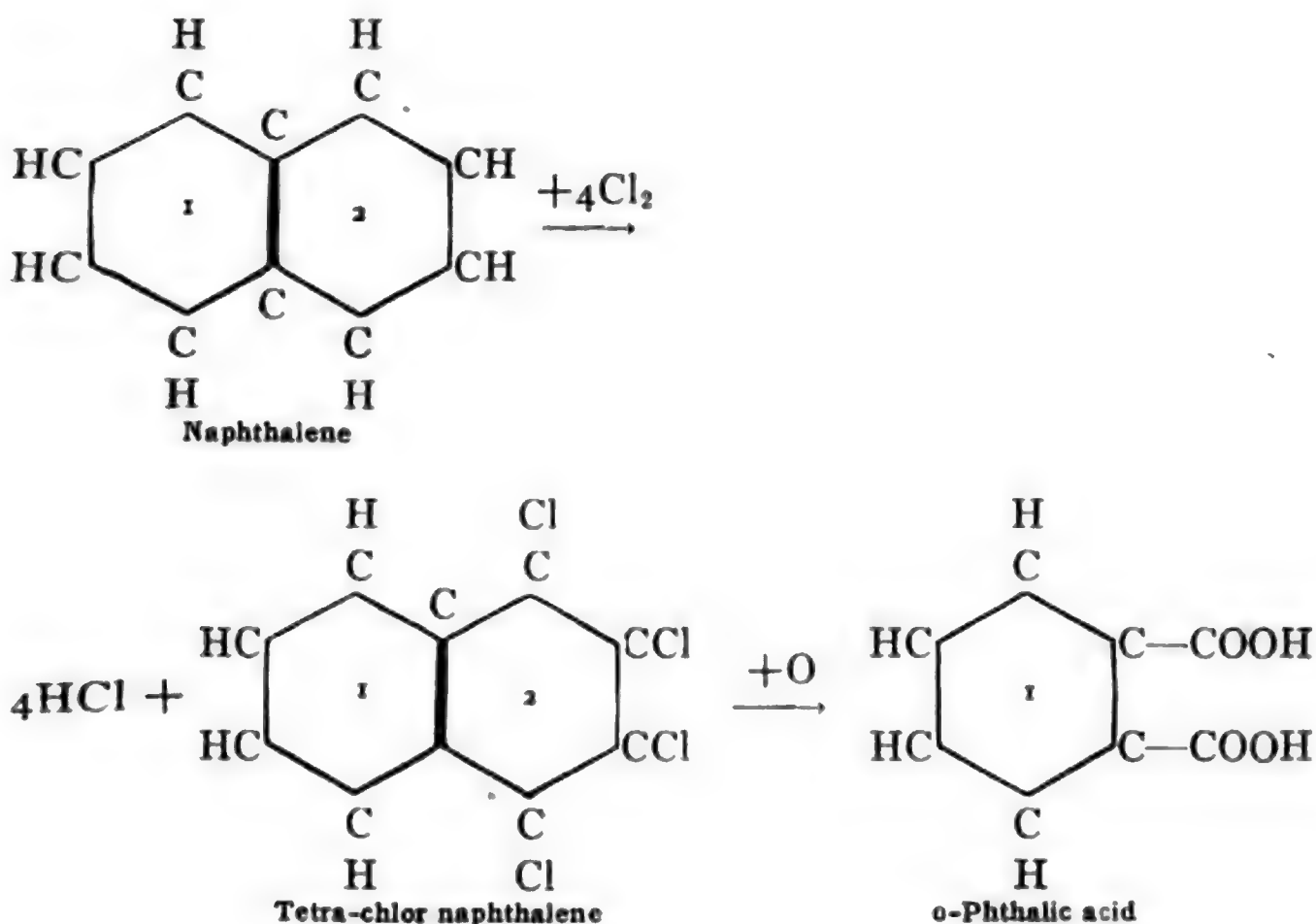


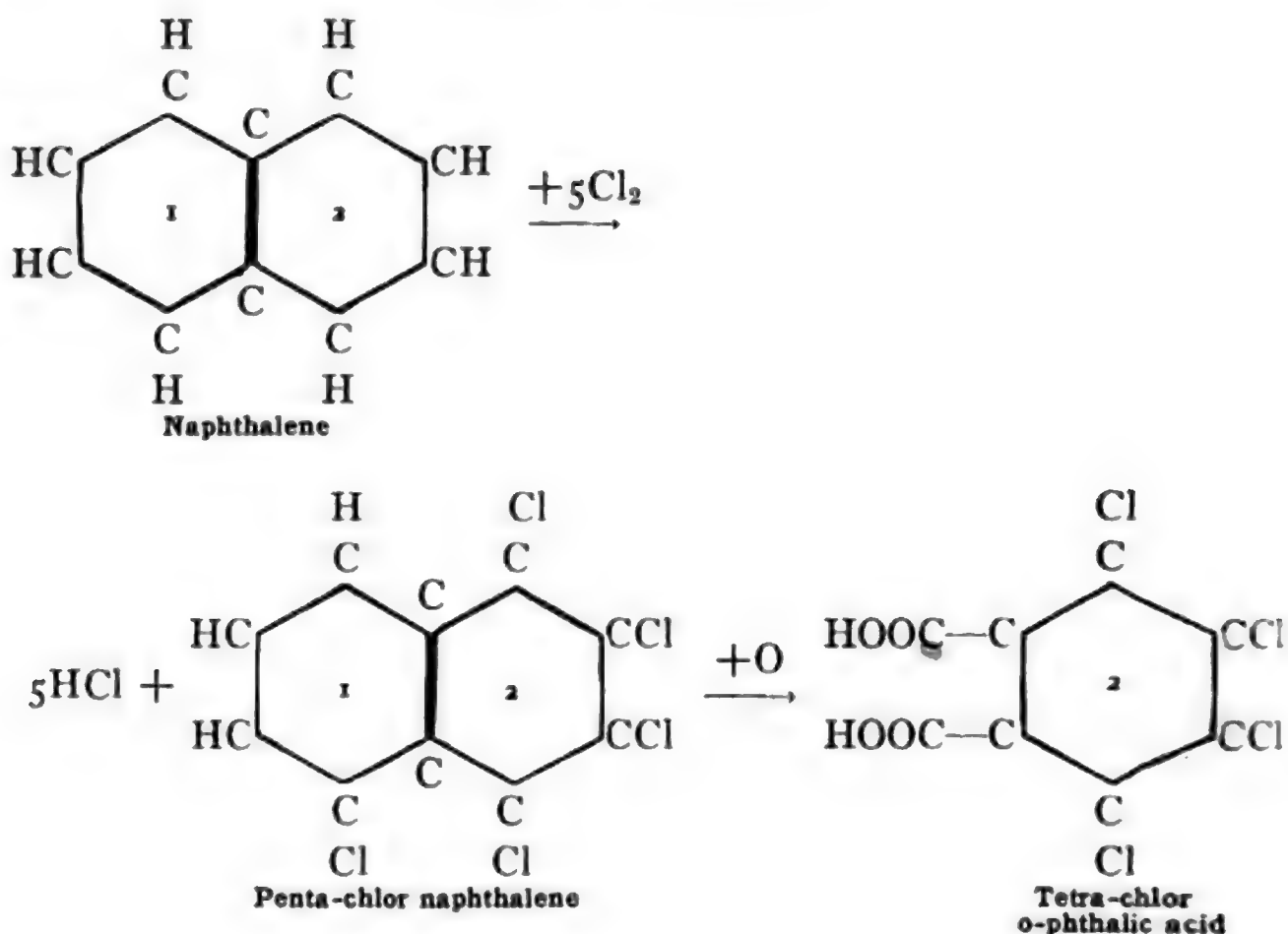
That is, there are two benzene rings condensed together by two carbons in common so that either one is a complete ring. The reactions of nitro naphthalene and amino naphthalene, may be represented as follows:



Either one of the nuclei indicated by 1 and 2 remains as a complete benzene ring in the products the other ring being destroyed. It is not really two benzene rings but, as it were, two such rings condensed in such a way that two carbon atoms are in common, so that while *only one complete ring exists either part of the compound may be this ring.*

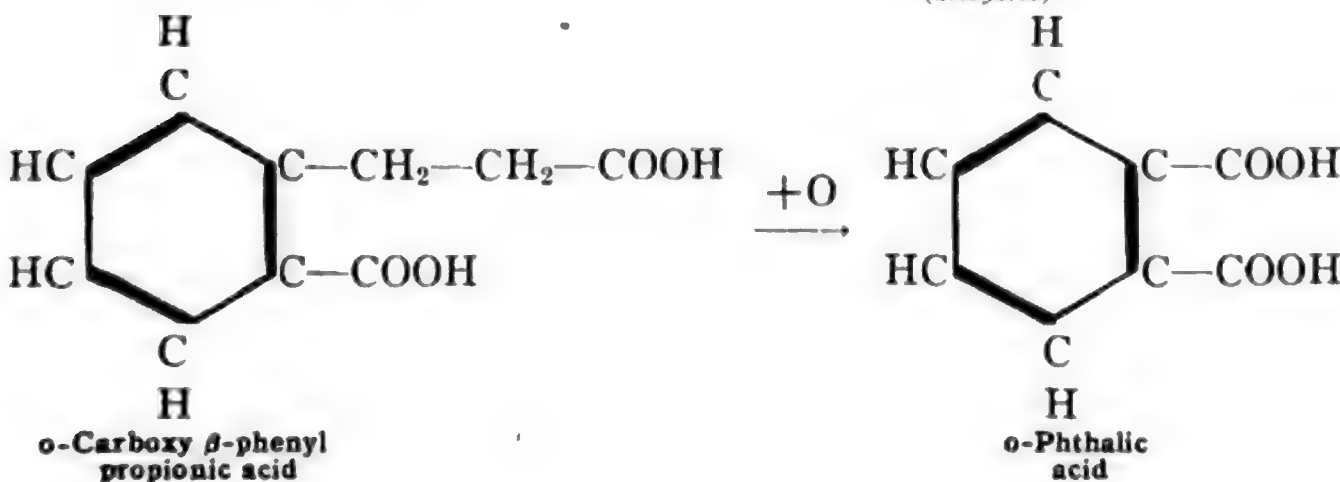
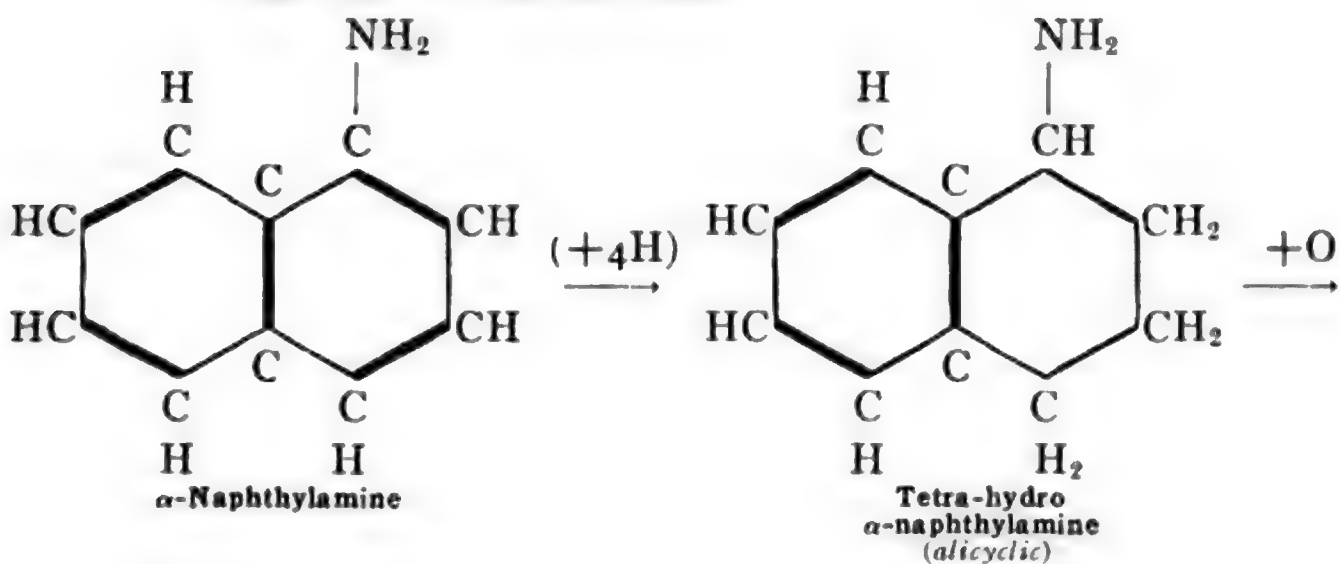
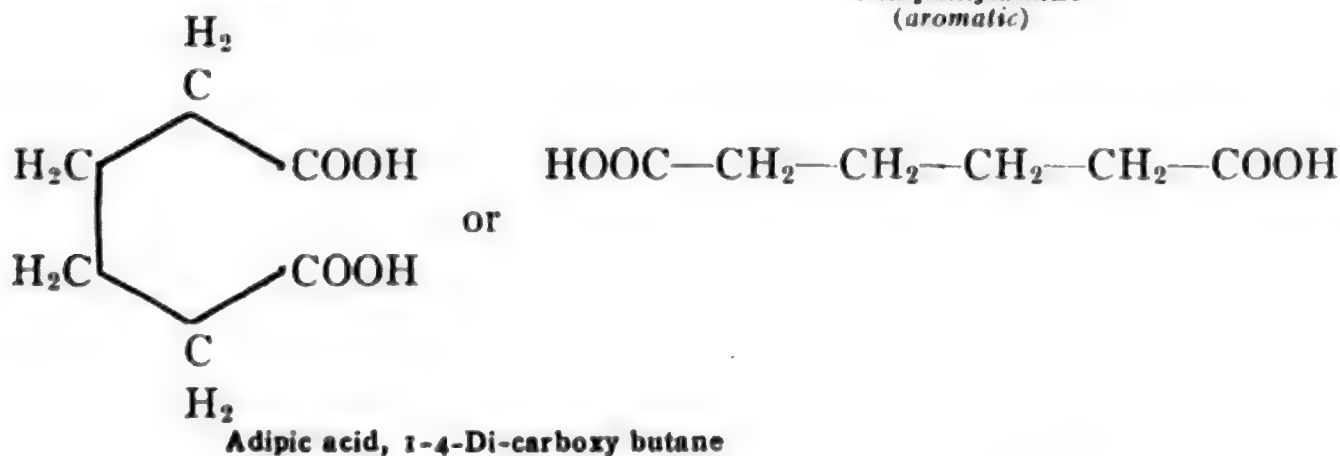
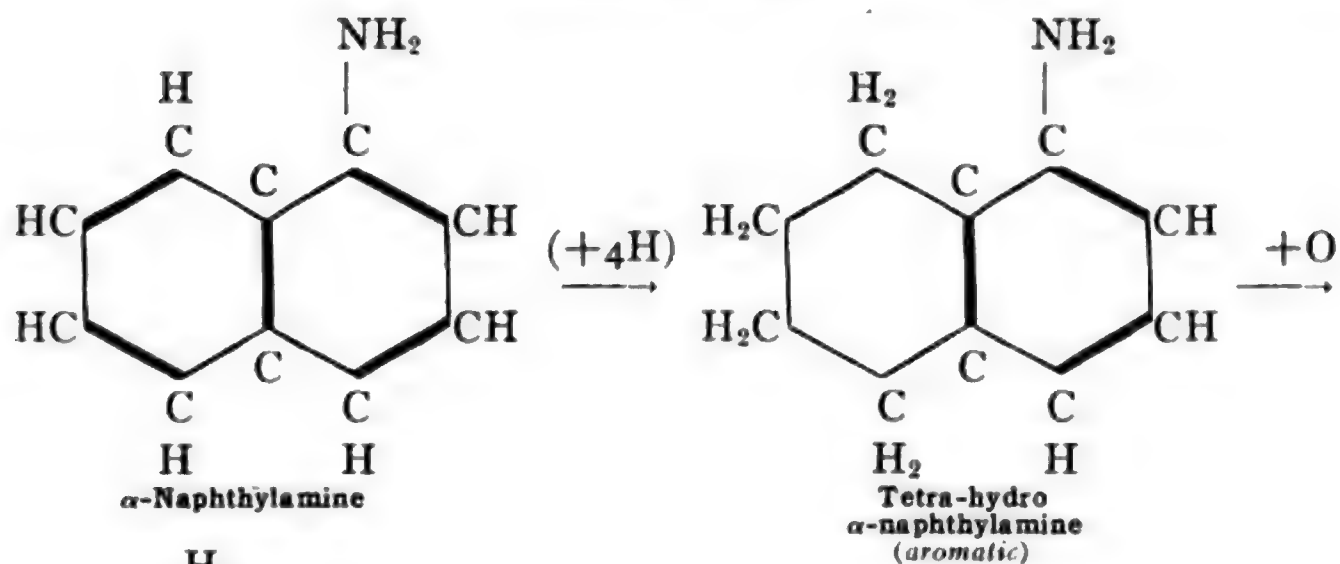
Chlor Naphthalenes.—Another series of reactions which support the view just discussed, that in naphthalene there are present two nuclei either one of which is a benzene ring, is found in **Laurent's** work on the chlorine substitution products of naphthalene. When naphthalene is chlorinated it yields different chlor naphthalenes. Two of these are important in this place, viz., a **tetra-chlor naphthalene**, $C_{10}H_4Cl_4$ and a **penta-chlor naphthalene**, $C_{10}H_3Cl_5$. Now the first one must have all four chlorines linked to one nucleus because on oxidation it yields **ortho-phthalic acid**, as below. The penta-chlor compound must of necessity have at least one of the chlorines linked to the second nucleus as only four are possible of being linked to one nucleus. Now this compound on oxidation yields not *mono-chlor* phthalic acid but *tetra-chlor* phthalic acid. The reactions may be represented as follows:





In the first case *one nucleus* remains as a *benzene ring* in phthalic acid while in the second case it must be the *other nucleus* which remains as a *benzene ring* in tetra-chlor phthalic acid. The proof here then is exactly the same as in the case of nitro naphthalene and amino naphthalene, viz., that in naphthalene *either nucleus is a benzene ring*.

Tetra-hydro Naphthylamines.—That at one time only one benzene ring is actually present in naphthalene is shown by the work of **Bamberger** on the **tetra-hydro naphthylamines**. **Mono-amino naphthalenes**, analogous to aniline, are called **naphthylamines**. These naphthylamines yield hydrogen addition products analogous to those formed from benzene (p. 811) or naphthalene. Now one of the naphthylamines, viz., **alpha-naphthylamine** (the isomerism will be discussed presently, (p. 775), yields two different products by the addition of four hydrogen atoms. That these two compounds are different and that the addition of four hydrogen atoms distinctly changes the character of the nucleus to which they are added is seen from the following reactions.



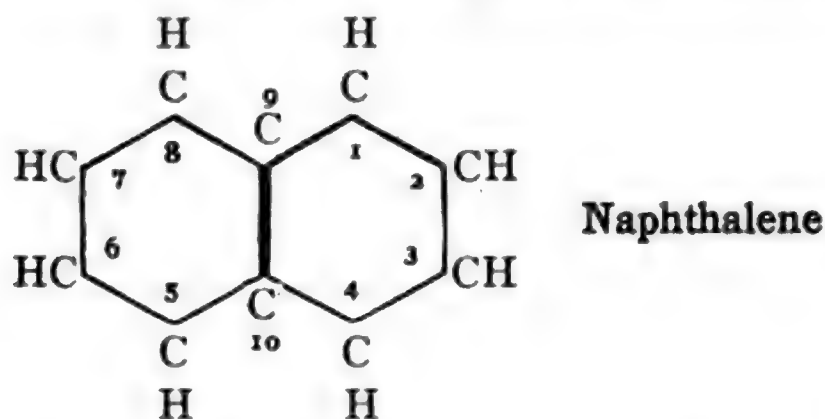
When **alpha-naphthylamine**, in amyl alcohol, is treated with sodium amalgam four hydrogens are added to the naphthyl amine. The tetrahydro naphthylamine obtained must have the four hydrogens added to the other nucleus than the one to which the amino group is linked because on oxidation an *aliphatic di-basic acid* is obtained containing four CH_2 groups and the amino group with the nucleus to which it was linked is destroyed yielding the two carboxyl groups. That this latter nucleus is a benzene ring is indicated by the fact that the tetrahydro naphthylamine possesses properties *like an aromatic amine, aniline*, and *not like an aliphatic amine, methyl amine, e.g.*, it readily undergoes the diazo reaction and is not ammoniacal in odor. On this account this particular tetrahydro naphthylamine and others similar to it are termed *aromatic tetra-hydro naphthylamines*. It will be seen that the addition of the four hydrogens to one of the nuclei makes that nucleus distinctly saturated or aliphatic in character as is shown by the formula and by the aliphatic acid resulting from oxidation. That is, the addition of hydrogen and conversion of a nucleus into a saturated ring makes it impossible for this nucleus to remain as a benzene ring when the other nucleus is destroyed. Thus only one nucleus is a benzene ring at any one time. That one of the two nuclei, and this may be either of the two, is a benzene ring has already been proven by the oxidation products of nitro naphthalene and amino naphthalene (p. 770) and is further proven by the second reaction above. The nucleus, which, in the first reaction, loses its benzene ring properties and yields an aliphatic acid, in the second reaction retains its benzene properties and yields an aromatic acid, **orthophthalic acid**. Also the nucleus containing the amino group is aromatic in the tetra-hydro compound in the first reaction but becomes alicyclic in the isomeric compound in the second reaction, yielding on oxidation a three carbon aliphatic chain in **ortho-carboxy β -phenyl propionic acid** (p. 697). The aliphatic character of the nucleus to which the amino group is linked in the second tetra-hydro product is shown by the fact that this compound is *like aliphatic amines* in character, *i.e.*, it is strongly ammoniacal in odor and does not undergo diazotization. It is termed an *alicyclic tetra-hydro naphthylamine*.

Thus the final conclusion in regard to the constitution of naphthalene is that it consists of one benzene ring with a four carbon chain of (CH) groups linked by its two end carbons to the ring in two positions

ortho to each other. As such a structure is symmetrical either part may be considered as the ring and the other as constituting the four carbon chain. Either nucleus may in fact remain as a benzene ring on the destruction of the other, but if, by the addition of hydrogen, the character of either nucleus is changed to that of a saturated ring it thus loses its benzene character and cannot remain as a benzene ring, the other nucleus, however, retaining its character as a true benzene ring. As the structure has the appearance of two benzene rings with one side of two carbon atoms in common it is usually referred to as a *condensed benzene ring compound*, i.e., two benzene rings condensed together into one compound.

DERIVATIVES

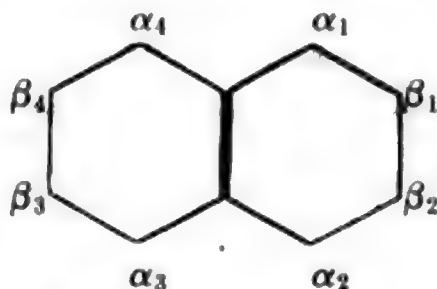
Isomerism.—From the condensed ring structure of naphthalene we should expect at least as great possibility of isomerism in its derivatives as was found in the case of derivatives of benzene. The fact is that the possibility of isomerism is much greater. As was done in the case of the single benzene ring we may arbitrarily number the positions in the naphthalene formula. The numbering generally accepted is as follows:



It will be observed that substitution or addition may take place in any or all of the positions 1, 2, 3, 4, 5, 6, 7, 8, while in positions 9 and 10 addition only is possible.

Mono-substitution Products, alpha and beta.—In the benzene ring we found that no isomeric mono-substitution products are known and according to the hexagon formula none are possible. With naphthalene, however, *two isomeric mono-substitution products* are known in all classes of derivatives. Examination of the formula shows that this is possible. Positions 1, 4, 5, 8 are alike and when substitution in one of these positions takes place the product is designated as an *alpha* compound. These four positions are different from the remaining four, viz., 2, 3, 6,

7, which are also alike and which are designated as the *beta* positions. In case there is a second substituting group, and the terms *alpha* and *beta* are used, the four positions in each set are also numbered as follows:



Di-substitution Products.—Usually however the di-substitution products are designated by numbers as first indicated. The names *ortho*, *meta* and *para* are also sometimes used exactly as in the benzene products together with other similar names applying to definite pairs of positions. By examining the formula we shall find that *ten isomeric di-substitution products* of naphthalene are possible in case the two substituents are the same. These ten with their numerical designations and names are as follows:

- (1) 1-2 or α_1 - β_1 ; (3-4 or β_2 - α_2 ; 5-6 or α_3 - β_3 ; 7-8 or β_4 - α_4) are all *ortho*
- (2) 2-3 or β_1 - β_2 ; (6-7 or β_3 - β_4) are also *ortho*
- (3) 1-3 or α_1 - β_2 ; (2-4 or β_1 - α_2 ; 5-7 or α_3 - β_4 ; 6-8 or β_3 - α_4) are all *meta*
- (4) 1-4 or α_1 - α_4 ; (5-8 or α_3 - α_4) are *para*
- (5) 1-8 or α_1 - α_4 ; (4-5 or α_3 - α_4) are *peri*
- (6) 1-5 or α_1 - α_3 ; (4-8 or α_3 - α_4) are *ana*
- (7) 1-6 or α_1 - β_3 ; (4-7 or α_2 - β_4 ; 2-5 or β_1 - α_2 ; 3-8 or β_2 - α_4) are *epi*
- (8) 1-7 or α_1 - β_4 ; (4-6 or α_2 - β_3 ; 3-5 or β_2 - α_3 ; 2-8 or β_1 - α_4) are *kata*
- (9) 2-6 or β_1 - β_3 ; (3-7 or β_2 - β_4) are *amphi*
- (10) 2-7 or β_1 - β_4 ; (3-6 or β_2 - β_3) are *pros*

In case the two substituents are different four additional isomers are possible, as indicated by the underscored pairs of positions, making a total of fourteen. These are all known in the case of the mixed amine and sulphonic acid naphthalenes (p. 786). We may simply state that in case like substituents enter the naphthalene the possibilities are:

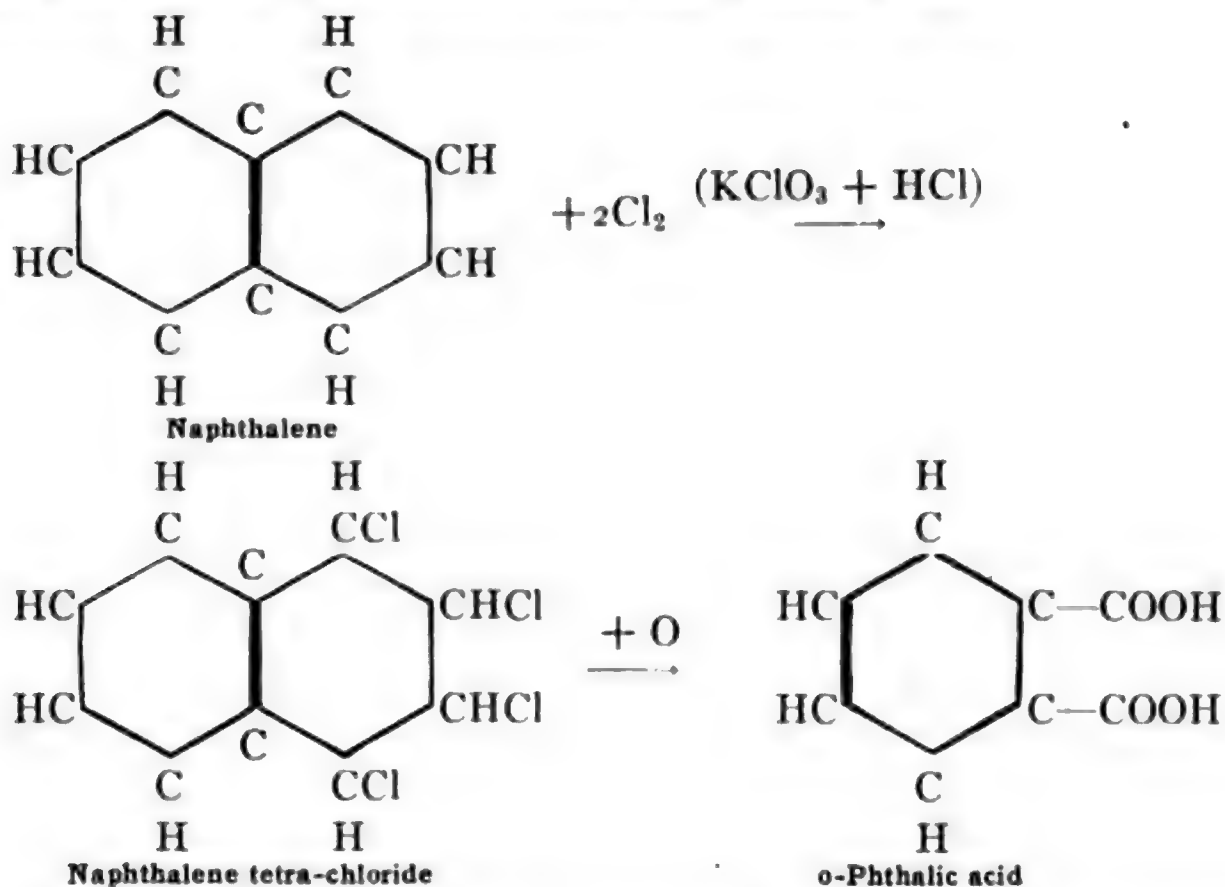
tri-substituted naphthalenes.....	14
tetra- substituted naphthalenes.....	22
penta-substituted naphthalenes.....	14
hexa-substituted naphthalenes.....	10
hepta-substituted naphthalenes.....	2
octa-substituted naphthalenes.....	1

Thus we can see how numerous are the possible isomers among the derivatives of naphthalene.

Halogen Derivatives

Substitution Products.—The halogen derivatives of naphthalene include both substitution and addition products. The tetra- and penta-chlor substituted naphthalenes have already been referred to as furnishing proof that in naphthalene there are present two benzene nuclei (p. 771). Other halogen substituted naphthalenes are known but none need be discussed in detail.

Addition Products.—The halogen addition products of naphthalene are more easily formed than are the substitution products. The tetra-chlor compound is of special interest and has been referred to. We have stated that naphthalene is oxidized to *ortho*-phthalic acid. This oxidation was originally carried out not with naphthalene itself but with **naphthalene tetra-chloride**, $C_{10}H_6Cl_4$. When naphthalene is treated with chlorine (potassium chlorate, $KClO_3$ and hydrochloric acid HCl), addition takes place and the *tetra-chlor addition product* is formed. By the further action of the chlorine, as an oxidizing agent, the tetra-chloride is converted into *ortho*-phthalic acid.

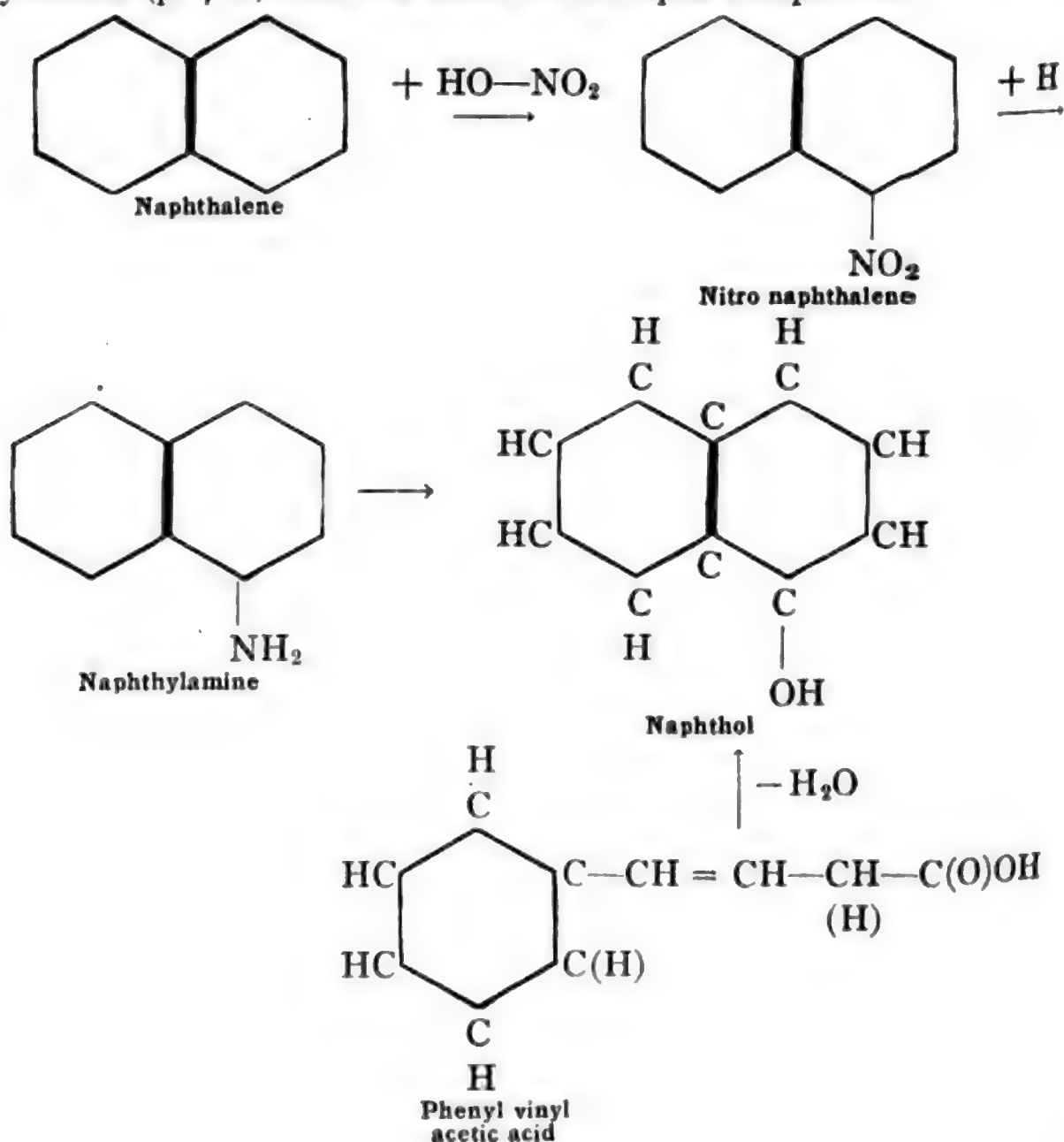


This reaction is easily carried out in the laboratory and is a common

exercise. For a long time it was the commercial method of converting naphthalene into phthalic acid but it has been replaced by the oxidation of naphthalene with sulphuric acid in the presence of a catalytic salt as previously stated (p. 766).

Nitro Naphthalenes

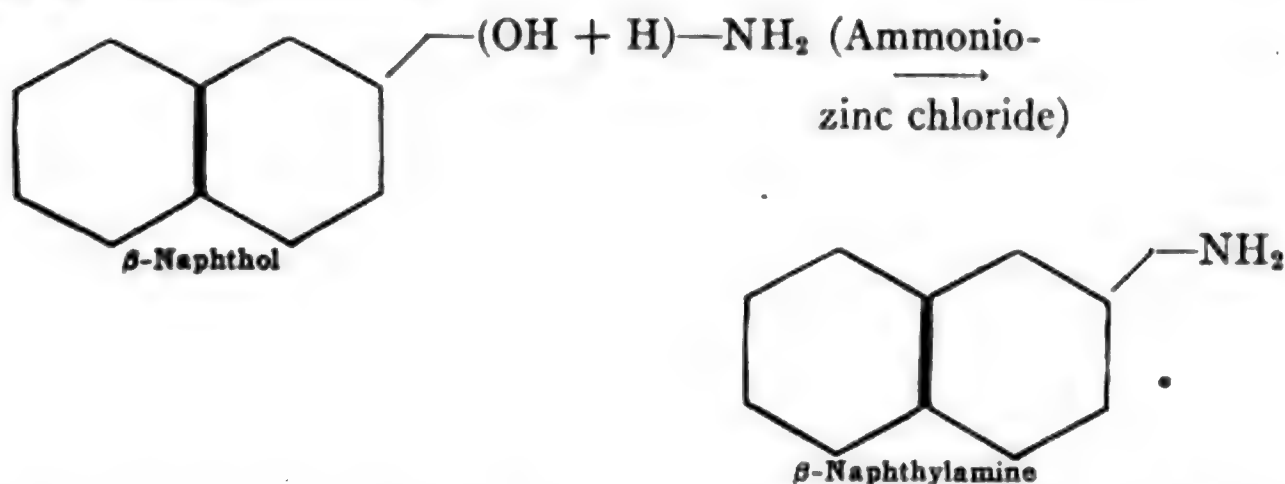
The nitro substitution products of naphthalene are easily prepared by the action of nitric acid on the hydrocarbon. By such direct nitration the product obtained is **alpha-nitro naphthalene**. This is proven by the following series of reactions. **Nitro-naphthalene** by reduction yields **amino naphthalene**, **naphthylamine**, which by the diazo reaction yields **hydroxy naphthalene**, **naphthol**. Now the naphthol so obtained is identical with the one resulting from the **phenyl vinyl acetic acid** synthesis (p. 768) and this must be the *alpha* compound.



In the naphthalene derivatives the identification of a compound as an *alpha* substitution product is usually accomplished by converting it into one of the compounds above.

Naphthylamines, Amino Naphthalenes

Synthesis from Naphthols.—The *mono-amino substitution products* of naphthalene are known as **naphthylamines**. Two such compounds are known, viz., an *alpha* and a *beta*. Each may be prepared by the reduction of the corresponding **nitro naphthalene**, and also from the corresponding hydroxy naphthalene or **naphthol** by treatment with ammonio-zinc chloride or ammonio-calcium chloride. These two reagents are made by passing ammonia gas over anhydrous zinc chloride or anhydrous calcium chloride. On heating they each yield ammonia and the anhydrous salt. They are thus common reagents for effecting the action of ammonia at high temperatures and at the same time causing the elimination of water due to the action of the anhydrous zinc or calcium chloride.



This same reaction may be brought about by heating the naphthol with ammonium chloride and sodium hydroxide in an autoclave at 160° for two or three days. This formation of an amino derivative from a hydroxyl derivative by means of ammonia does not usually take place though it is possible to make aniline from phenol in this way.

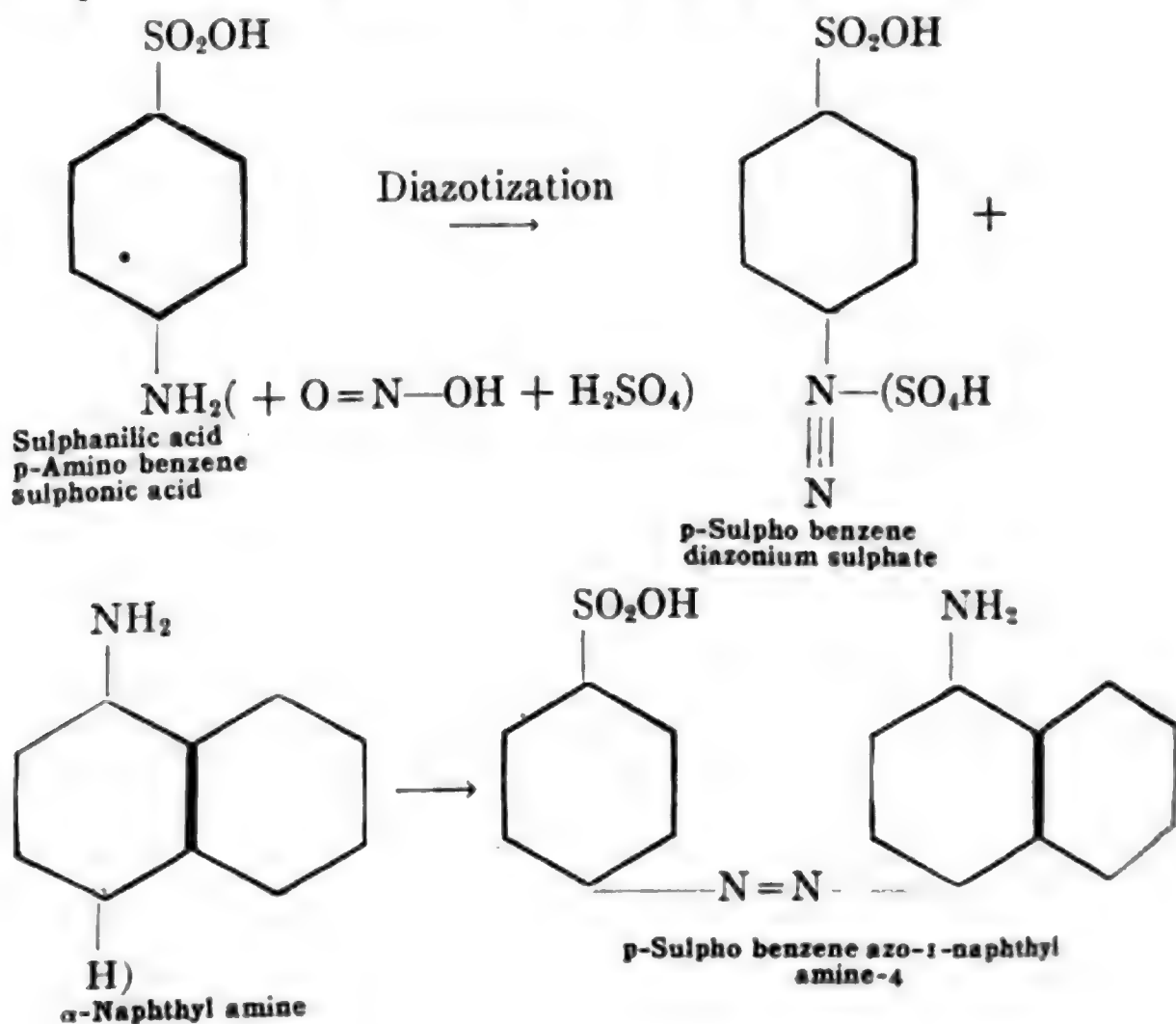
alpha-Naphthylamine.—**alpha-Naphthylamine** is a solid melting at 50° . It usually possesses a strong fecal-like odor though it is claimed to be odorless when pure. The salts react with a solution of ferric chloride giving a blue precipitate.

beta-Naphthylamine.—**beta-Naphthylamine** is also solid, m.p. 112° , with a slight odor. Salts of this amine do not cause any precipitate with solutions of ferric chloride.

Relation to Dyes.—The importance of the naphthylamines is due to the fact that they are intermediate products in the preparation of many valuable dyes especially of the azo dye series.

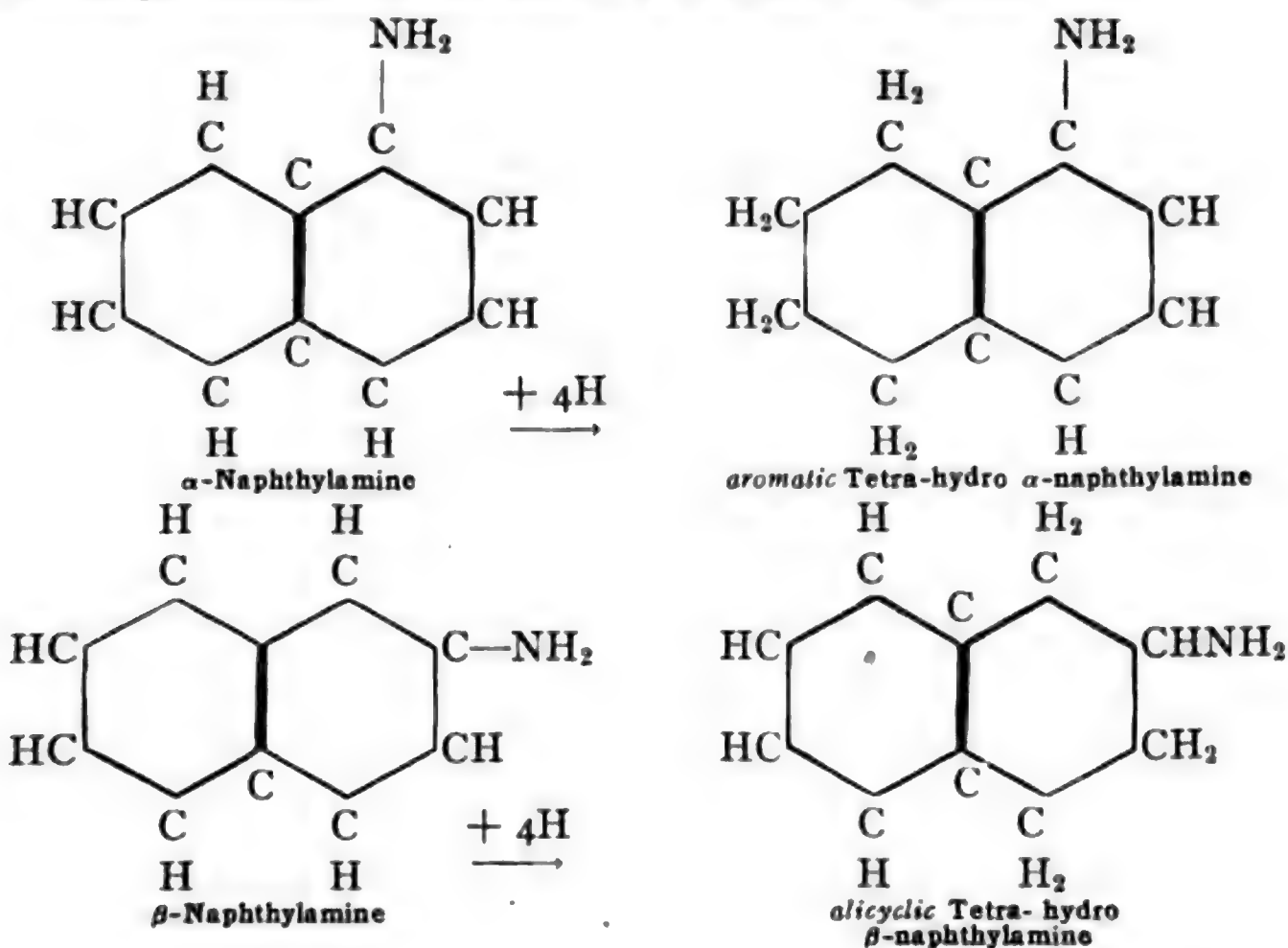
Diazotization.—Like aniline and other aromatic primary amines they undergo *diazotization*. The resulting diazo compounds undergo the various diazo reactions (p. 601) by means of which the naphthalene group becomes coupled as an *azo compound* with other naphthalene or benzene rings. These azo compounds are dyes. The most important dyes of this group are derived from mixed *amino and sulphonic acid* or mixed *amino and hydroxyl* derivatives of naphthalene and will be considered a little later. Not only, however, may the naphthylamines yield diazo compounds and through them azo compounds but they may be coupled as azo compounds with a diazotized benzene compound.

Reagent for Nitrites in Water.—An illustration of such a reaction is one which is the basis of the *colorimetric determination of nitrites in water*. When **sulphanilic acid, para-amino benzene sulphonic acid**, is diazotized and the resulting diazo compound treated with **alpha-naphthylamine** the benzene ring and the naphthalene ring become coupled as an azo compound which is red in color.



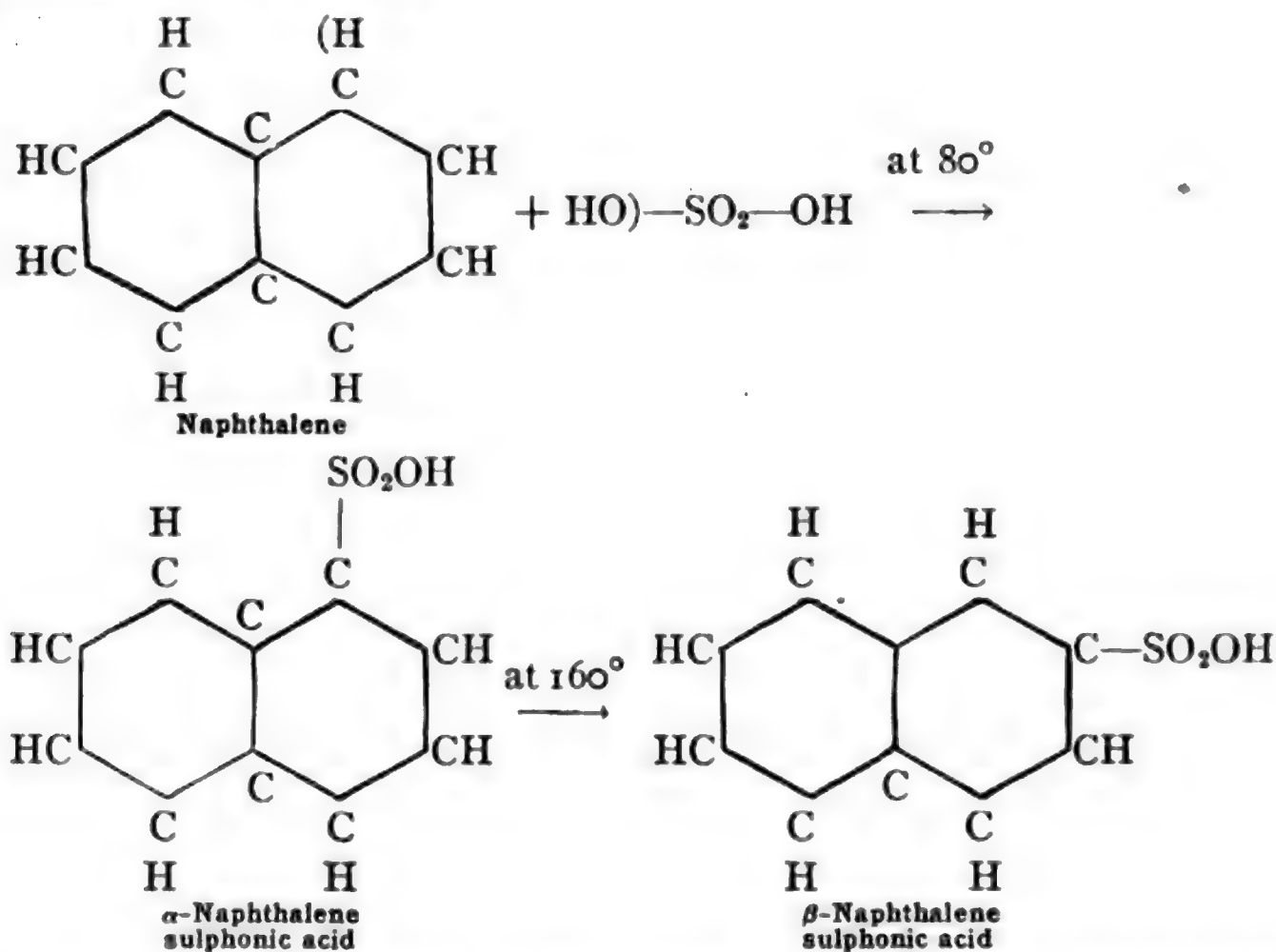
When a small amount of nitrites is present in water and the reagent of mixed **sulphanilic acid** and **alpha-naphthylamine** is added in the presence of sulphuric acid, the acid first reacts with the nitrites forming nitrous acid. The above diazo reaction and the coupling with the naphthylamine then take place slowly with the production of a red color in the solution. The depth of the color thus produced, on comparison with the color obtained with standard nitrite solutions, gives the means for calculating the amount of nitrites in the original water.

Hydrated Naphthylamines.—We have referred to the *hydrated naphthylamines* in our discussion of the constitution of naphthalene (p. 772). The tetra-hydro products are of two kinds: (1) Those termed *aromatic* in which the hydrogen is added to the benzene nucleus which does *not* contain the amino group and which possess the characters of *aromatic amines*. (2) Those termed *alicyclic* in which the hydrogen is added to the benzene nucleus which *does* contain the amino group and which possess the characters of *aliphatic amines*. Now while the *alpha*- and *beta*-naphthylamines each yield both kinds of tetra-hydro products if subjected to proper treatment yet by the same treatment, viz., with sodium amalgam in amyl alcohol, the *alpha*-naphthylamine yields an *aromatic* tetra-hydro compound while the *beta*-naphthylamine yields mostly an *alicyclic* compound.



Naphthalene Sulphonic Acids

Naphthalene like benzene is readily sulphonated by the direct action of sulphuric acid. When the reaction takes place at moderate temperatures, about 80° , the product is mostly the *alpha* compound while at higher temperatures, about 160° , the *beta* compound is formed, the *alpha*-naphthalene sulphonic acid being transformed into its *beta* isomer at this temperature.



Not only mono-sulphonic acids but also di- and tri-sulphonic acids are known. These all undergo the general reactions of the class as discussed under the sulphonic acid derivatives of benzene (p. 519). On fusion with potassium hydroxide they yield hydroxyl derivatives and similar fusion with potassium cyanide converts them into acid nitriles. They are characterized as soluble compounds and are readily coupled with diazo compounds yielding azo compounds many of which are dyes.

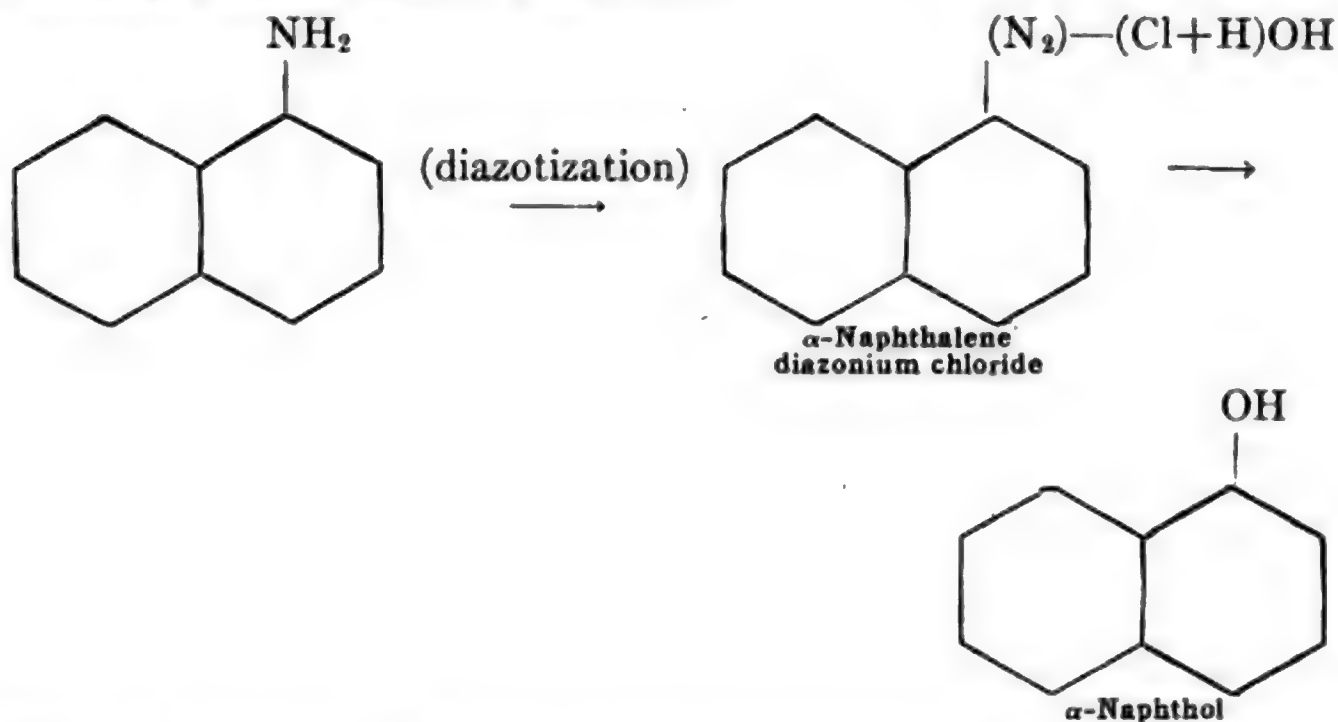
Naphthols, Hydroxy Naphthalenes

The **hydroxy naphthalenes** are known as **naphthols**. They possess a phenol-like odor and are exactly analogous to the phenols both in

methods of preparation and in properties. The hydroxyl group, however, is more reactive than in the benzene analogue. When fused with potassium hydroxide together with a metallic oxide the naphthols are oxidized to phthalic acid and benzoic acid.

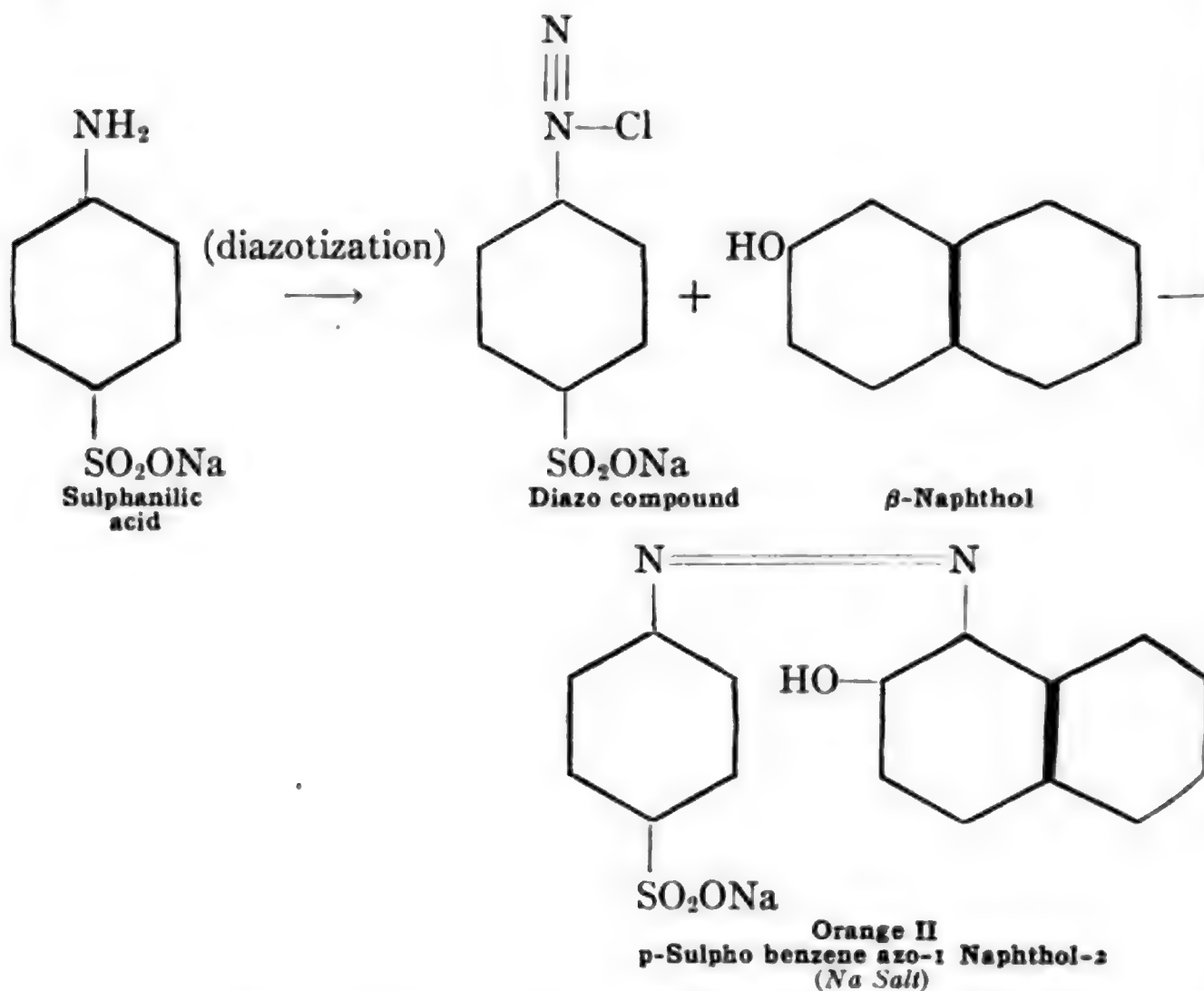
Synthesis from Naphthalene Sulphonic Acids.—The simplest method of synthesis is from the corresponding **naphthalene sulphonic acid** by fusion with potassium hydroxide.

From Naphthylamines.—They may also be prepared from the **naphthylamines** by diazotizing the amine and then decomposing the resulting diazo compound with water.

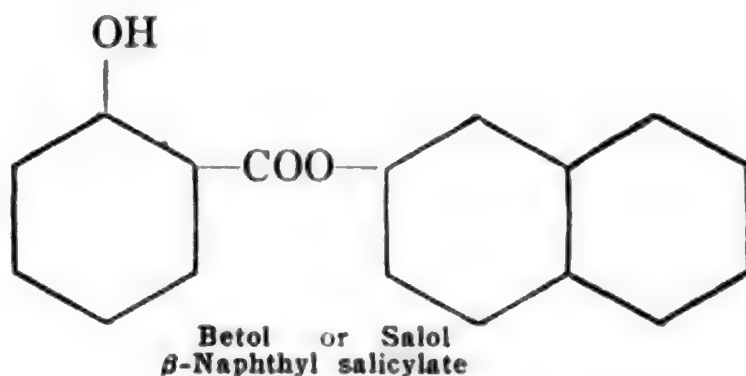


While this reaction may be used it is more customary, especially in the case of the *beta* compounds, to effect the reverse result, viz., to prepare the amine from the hydroxyl compound by the action of ammonia in the form of ammonio-zinc chloride as already discussed (p. 779).

Dyes, Orange II.—The naphthols yield important derivatives many of which are valuable as dyes. Most of the naphthol dyes are derivatives of mixed *naphthol sulphonic acid* or *nitro naphthol* compounds. These will be considered later. One important dye, however, is an *azo* derivative of *beta*-naphthol. It is analogous to the red colored compound formed in the test for nitrites in water (p. 780) and is prepared by treating **beta-naphthol** with the *diazo* compound of **sulphanilic acid**, **para-amino benzene sulphonic acid**, the naphthol being coupled to the benzene ring as an *azo* compound. It is an orange dye known as **Orange II** and is used in dyeing wool.



Betol. Salol.—Another simple derivative of *beta*-naphthol is the **beta-naphthyl ester of salicylic acid** analogous to oil of wintergreen, the methyl ester. It is another of the derivatives of this acid which has valuable medicinal properties. It is known as **betol**, also medicinally as **salol**.



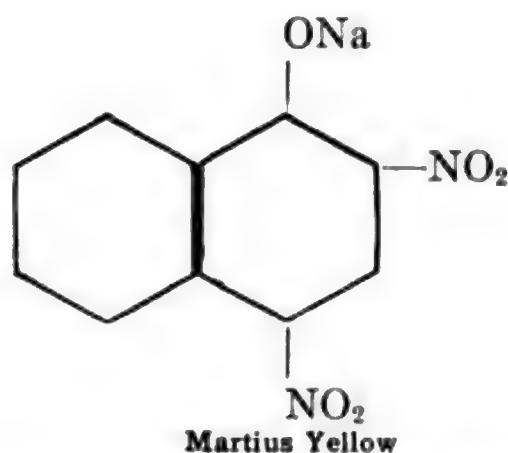
MIXED SUBSTITUTION PRODUCTS OF NAPHTHALENE

We have mentioned the fact that most of the dyes derived from naphthalene are mixed derivatives, *i.e.*, those in which more than one kind of group is substituted in the naphthalene molecule.

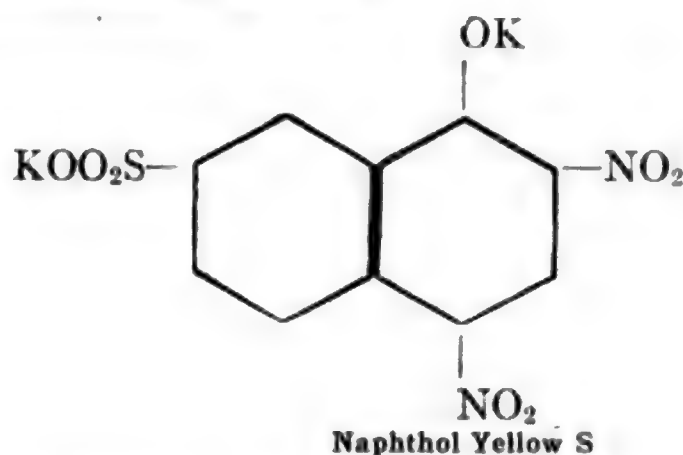
Nitro Naphthols

The simplest derivatives of this mixed character which yield dyes are the **nitro naphthols**, *i.e.*, mixed nitro and hydroxyl substitution products. Recalling well-known compounds of the benzene series it will be remembered that whereas mono-nitro benzene has practically no color, and di-nitro-benzene only a faint yellow color, the mixed tri-nitro phenol or **picric acid** has an intense yellow color and was one of the first yellow dyes used.

Martius Yellow.—In a similar way the nitro naphthalenes are only faintly colored and are not valuable as dyes while the mixed nitro and hydroxy naphthalenes are colored compounds. One of these is a yellow dye which was formerly used to dye wool and silk but is now principally used in dyeing soaps. It is the **2-4-di-nitro 1-naphthol** which in the form of its sodium, calcium or ammonium salt is known as **Martius yellow**.



Naphthol Yellow S.—A sulphonic acid derivative of this, *viz.*, **2-4-di-nitro 1-naphthol 7-sulphonic acid** in the form of the potassium salt is known as **Naphthol Yellow S**.

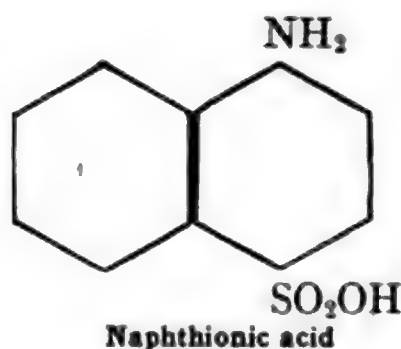


It is a yellow dye faster in color than the preceding and is used to dye wool and silk.

Naphthylamine Sulphonic Acids and Naphthol Sulphonic Acids

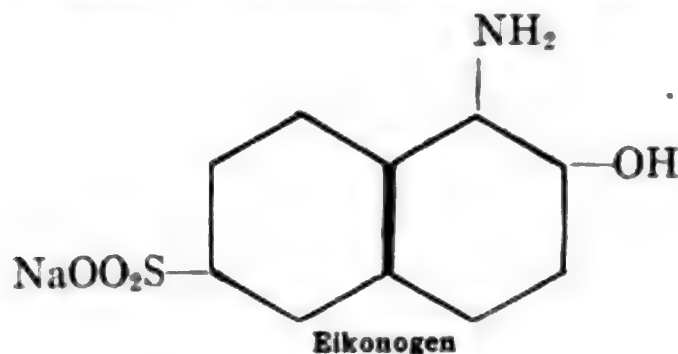
The amino-sulphonic acid derivatives of naphthalene known as naphthylamine sulphonic acids are interesting because of the support they give to our ideas in regard to the constitution of naphthalene and the possible isomeric di-substitution products. The mono-amino mono-sulphonic acid naphthalene being a di-substitution product, is, according to our theories, able to exist in fourteen possible isomeric forms (p. 776). It is a striking fact that with this particular compound *all fourteen isomers are known* thus giving strong support to our ideas in regard to the constitution of naphthalene.

Naphthionic Acid.—The most common and most important of these fourteen isomers is **1-naphthylamine 4-sulphonic acid**. It is known as **naphthionic acid**.



This compound is an important intermediate product in the preparation of dyes as will be explained presently.

Eikonogen.—A related compound, containing a hydroxyl group also, is a common photographic developer known as **eikonogen**. It is **1-amino 2-naphthol 6-sulphonic acid**, sodium salt.

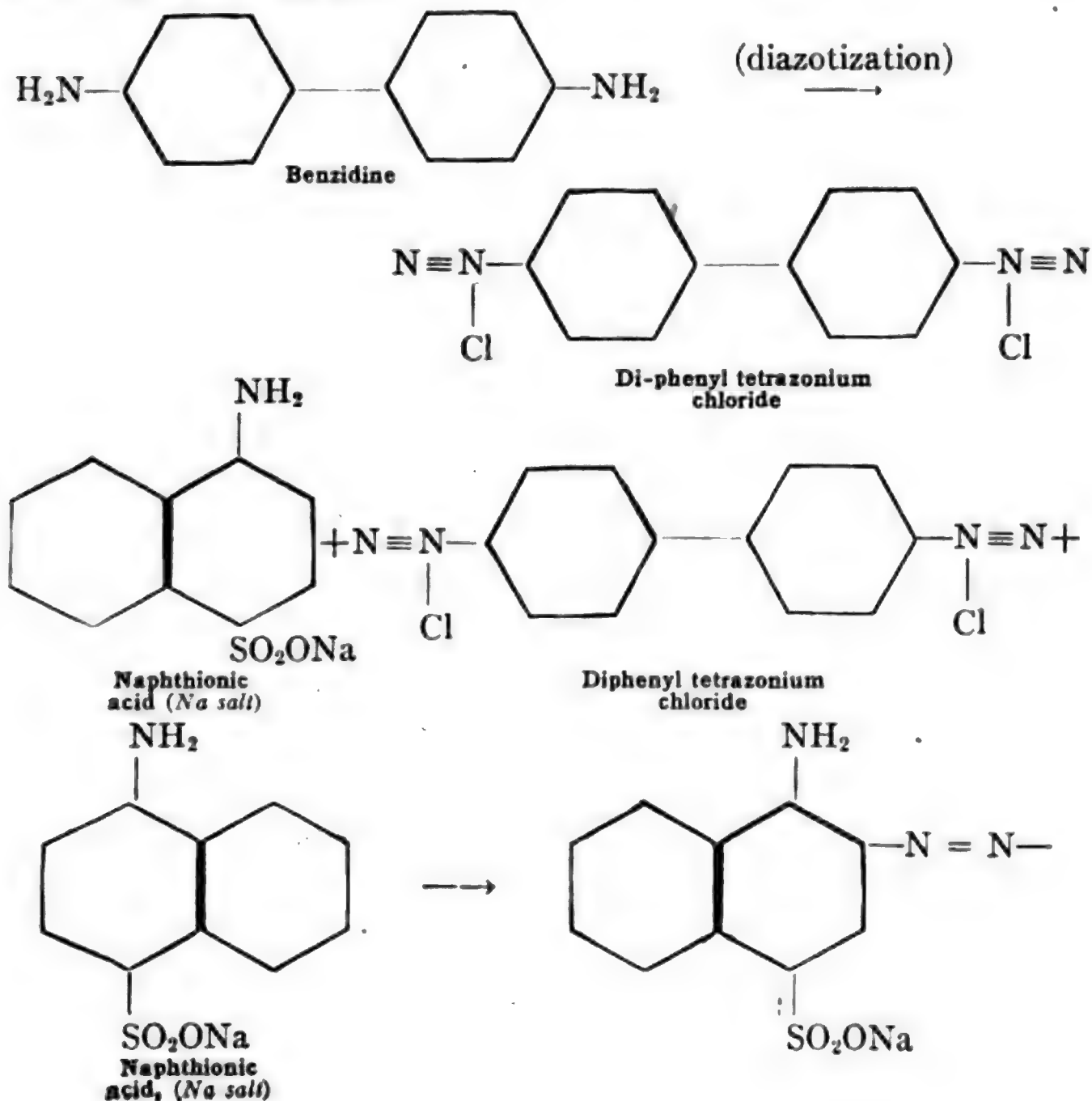


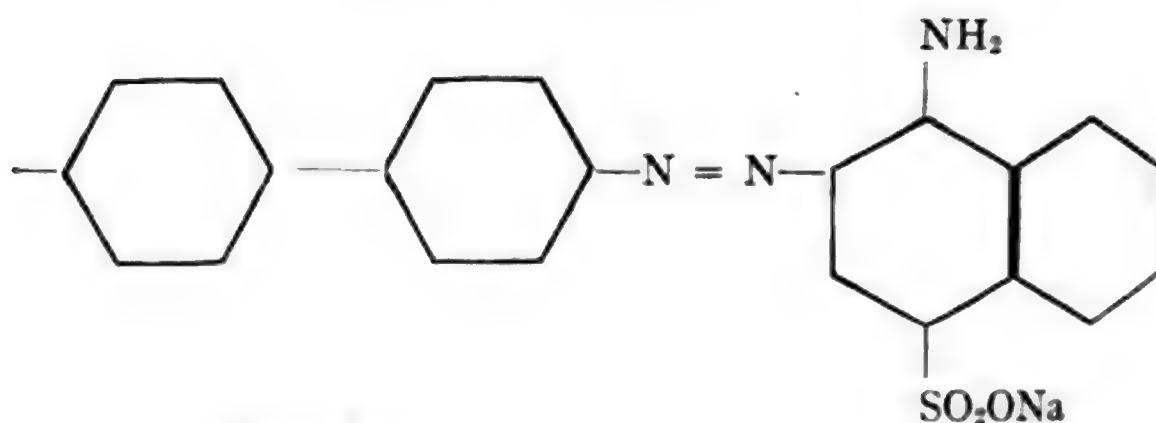
Azo Dyes from Naphthalene

The most important dyes derived from naphthylamine sulphonic acids and from naphthol sulphonic acids result from coupling them as azo compounds with other rings. This coupling is effected through a diazonium salt made by diazotizing an amine and bringing this di-

azonium salt in contact with the naphthalene compound. The amine which supplies the additional rings may be **aniline**, $\text{C}_6\text{H}_5\text{—NH}_2$, **benzidine**, $\text{H}_2\text{N—C}_6\text{H}_4\text{—C}_6\text{H}_4\text{—NH}_2$ (p. 732) **tolidine** $\text{H}_2\text{N—C}_6\text{H}_3\text{—(CH}_3\text{)—C}_6\text{H}_3\text{(CH}_3\text{)—NH}_2$ or **naphthylamine** itself. The best examples of this class of azo dyes derived from naphthalene which may be mentioned at this time are **Congo Red**, **Benzo-purpurin 4B**, **Naphthol Blue Black** and **Fast Red B**.

Congo Red.—When **benzidine** is diazotized a double diazo or *tetrazo* compound results (p. 575) from the diazotization of both of the amino groups. This diazonium or tetrazonium salt reacts with two molecules of **naphthylamine sulphonic acid**, **naphthionic acid**, forming a double azo or *disazo* compound. The sodium salt of this compound is Congo red. The reactions are:

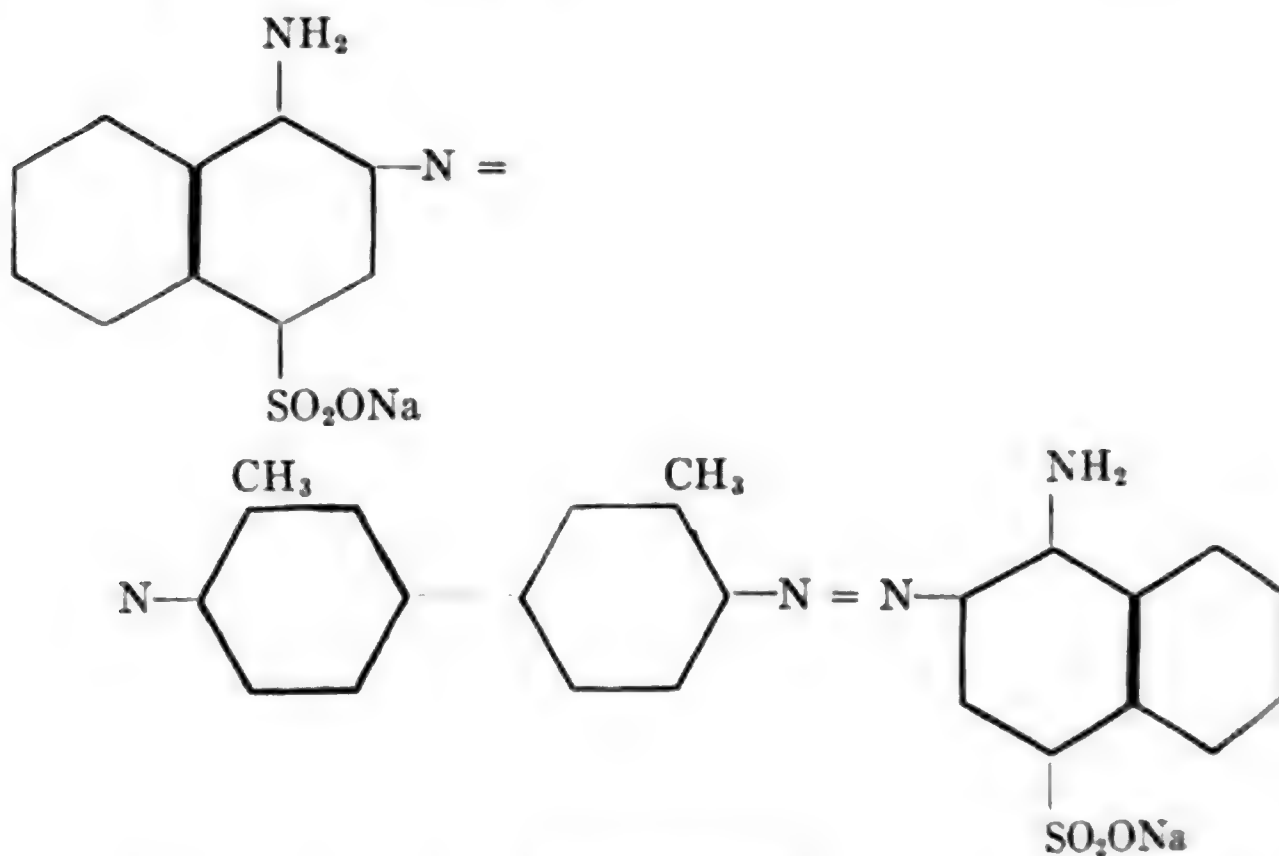




Congo Red

Congo red is a representative of a group of dyes known as *substantive dyes* which are able to dye cotton *without the use of a mordant*. It is of special interest historically as it was the first dye of this group to be made.

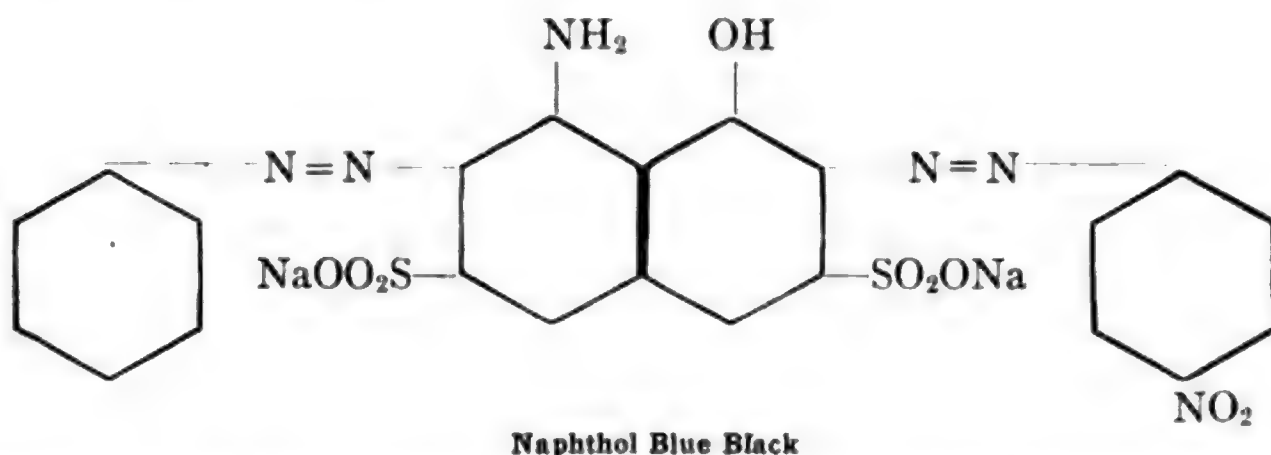
Benzo purpurin.—**Tolidine** is **di-methyl benzidine**, that is it bears the same relation to **toluene** and **ortho-toluidine** that benzidine does to benzene and aniline. When this is diazotized and the tetrazonium salt coupled with sodium naphthionate the *disazo* compound resulting is a dye known as **benzopurpurin 4B**, which is also a *substantive dye* of a red color.



Benzo-purpurin 4B

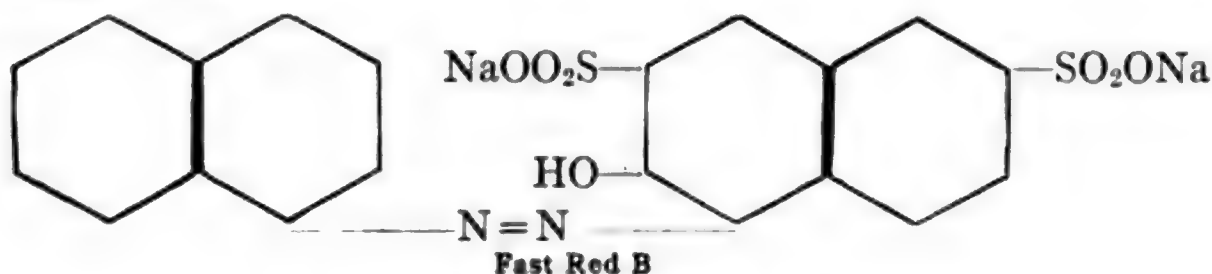
Naphthol Blue Black.—The dye known as **naphthol blue black** is an azo dye of the same general structure as the two preceding but

its components are more mixed in character. An amino naphthol sulphonic acid, viz., **1-amino 8-naphthol 3-6-di-sulphonic acid**, sodium salt, is coupled as a *disazo* compound on one side with a simple benzene ring and on the other with a *para-nitro* ring. The coupling is effected by means of diazotized aniline, **benzene diazonium chloride**, and by means of diazotized **paranitraniline**, **p-nitro benzene diazonium chloride**. The reactions being like those already given we need simply give the formula of the dye:



This dye is *not* a substantive dye. It dyes wool a blue black color.

Fast Red B, Bordeaux B.—One more example of an azo dye derived from naphthalene may be given in which naphthylamine is diazotized and coupled as an azo compound with a naphthol sulphonic acid. The compound **2-naphthol 3-6-di-sulphonic acid** is a dyestuff intermediate known as **R-salt** (red salt) because it is used in making red dyes. When **alpha-naphthylamine** is diazotized and coupled with R-salt the resulting azo dye is known as fast red B or Bordeaux B. Its constitution is



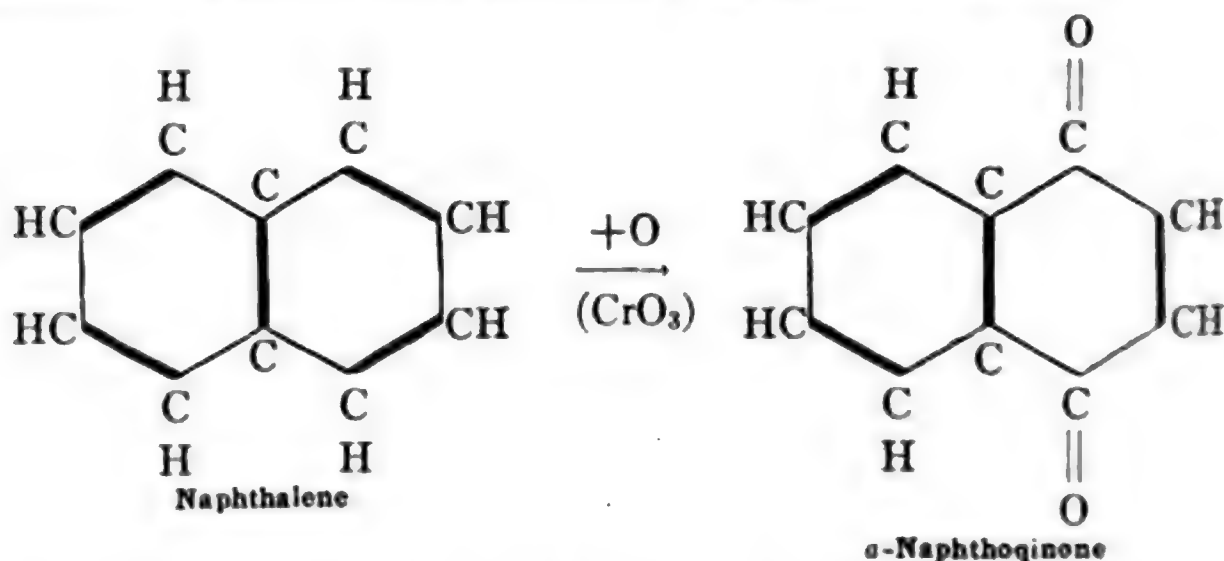
This dye also is *not* a substantive dye. It dyes wool red.

Illustrations of azo dyes containing naphthalene groups might be continued in very large number but this is undesirable as it would only tend to confuse the point to be emphasized, viz., that mixed amino or hydroxyl derivatives of naphthalene either by diazotization and coupling with other compounds, as in the case of **fast red**, or by coupling with

diazo compounds derived from other amines, such as aniline, benzidine, tolidine, etc., as in **Congo red**, etc., yield important *azo dyes*. As previously stated when the azo dyes were first mentioned (p. 576), the most important dyes of this class are those containing naphthalene groups. A very important sub-group of the azo dyes consists of the *substantive dyes* which are able to dye cotton without the use of a mordant. This is of great value technically. The great variety of the mixed naphthalene derivatives which may become component parts of such dyes is very large so that an almost endless variety of products is possible. In this discussion we see emphasized again the very great importance and commercial value of the diazo reactions.

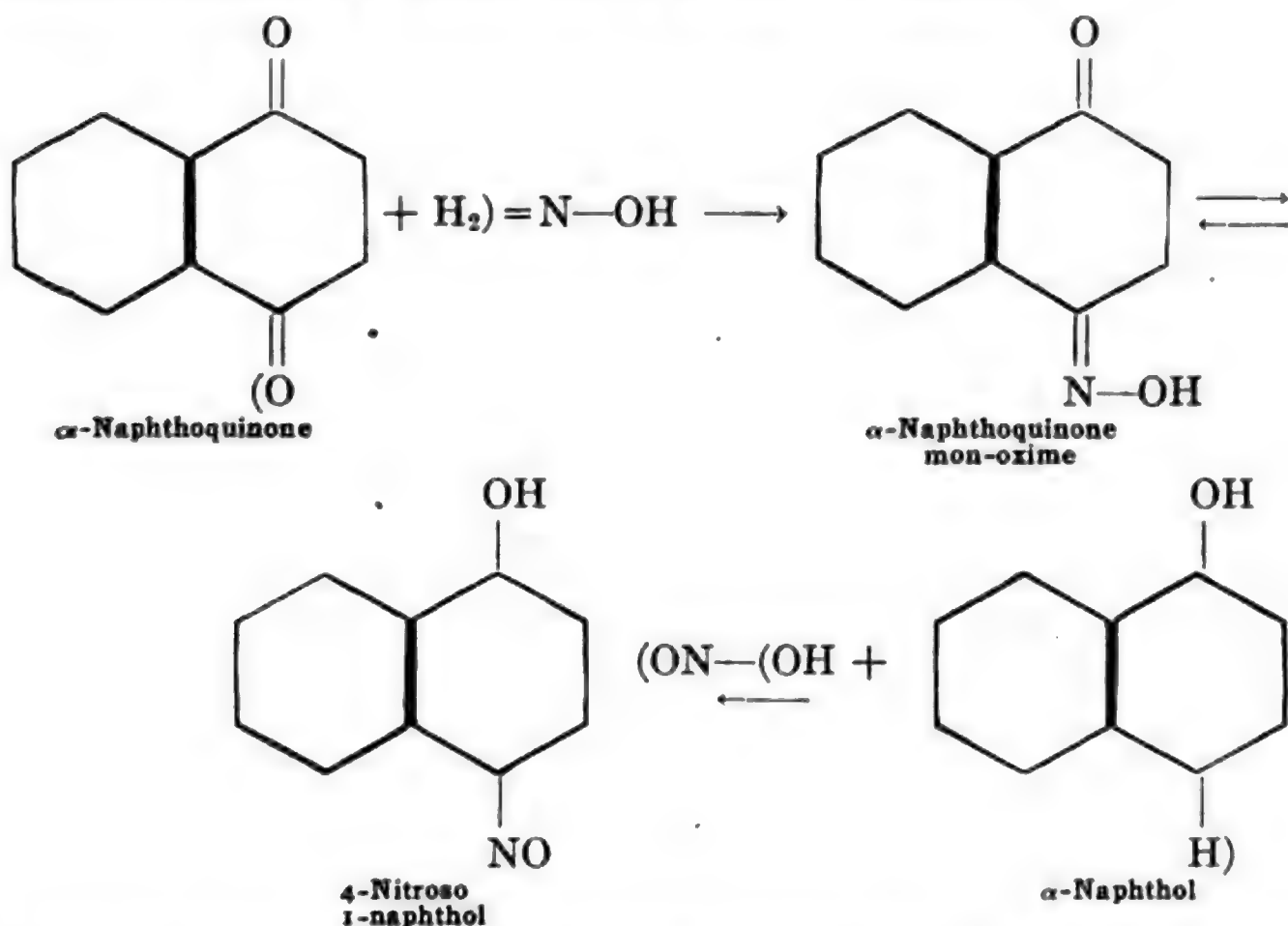
Naphthoquinones

It will be recalled that when **para-di-hydroxy benzene**, **hydroquinol**, and also other *para* di-substitution products of benzene are oxidized there is obtained the compound known as **quinone** or **benzoquinone** (p. 636). In a similar way *para* di-substituted naphthalenes, especially hydroxyl and amino compounds, and in fact naphthalene itself when oxidized with chromic acid, yield a quinone analogous to benzoquinone and which is known as **alpha-naphthoquinone**.



A **beta-naphthoquinone** is also obtained by the oxidation of **1-amino 2-naphthol** or other 1-2-di-substituted naphthalenes. In it the two carbonyl groups are formed with the *alpha* and *beta* carbons *ortho* to each other and it is analogous to *ortho*-benzoquinone. These naphthoquinones resemble the corresponding benzoquinone in their properties and reactions. **alpha-Naphthoquinone** is like benzoquinone in that it is yellow in color, has a strong odor and is volatile with steam.

beta-Naphthoquinone, on the other hand, is like *ortho*-benzoquinone in being odorless and non-volatile with steam. It is red in color. Both yield oximes with hydroxyl amine and the mono-oximes are like the mono-oximes of benzoquinone in being pseudo compounds with nitroso hydroxyl compounds (p. 640). When *alpha*-naphthoquinone is treated with hydroxyl amine the same compound is obtained as by the action of nitrous acid on *alpha*-naphthol. In the same way *beta*-naphthoquinone monoxime is pseudo with **2-nitroso 1-naphthol**.

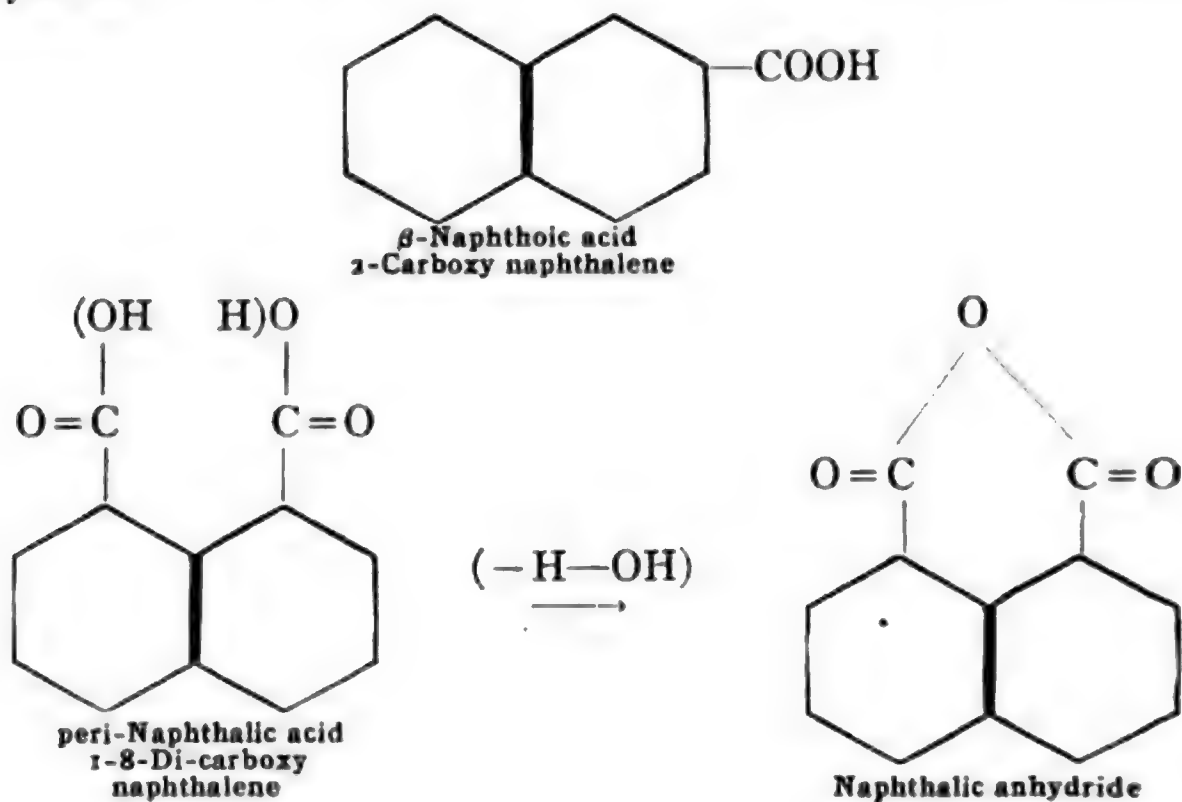


Both of the naphthoquinones yield *ortho*-phthalic acid on oxidation with nitric acid. The constitution of the naphthoquinones so far as the quinone containing ring is concerned is probably the same as that of benzoquinone (p. 636).

Naphthoic and Naphthalic Acids

By fusion of naphthalene sulphonic acids with potassium cyanide the corresponding cyano naphthalenes are obtained. These compounds are nitriles of naphthalene acids. The mono-carboxyl acids are known as **naphthoic acids** while the di-carboxyl acids are termed **naphthalic acids**. The naphthoic acids are similar to benzoic acid and the naphthalic acids are like the phthalic acids. The naphthalic acid

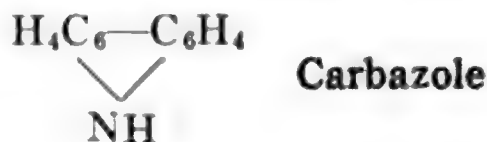
with the carboxyl groups in the 1-8 or *peri* positions is of especial interest because of its similarity to *ortho*-phthalic acid in readily yielding an anhydride.



ANTHRACENE AND DERIVATIVES

Anthracene

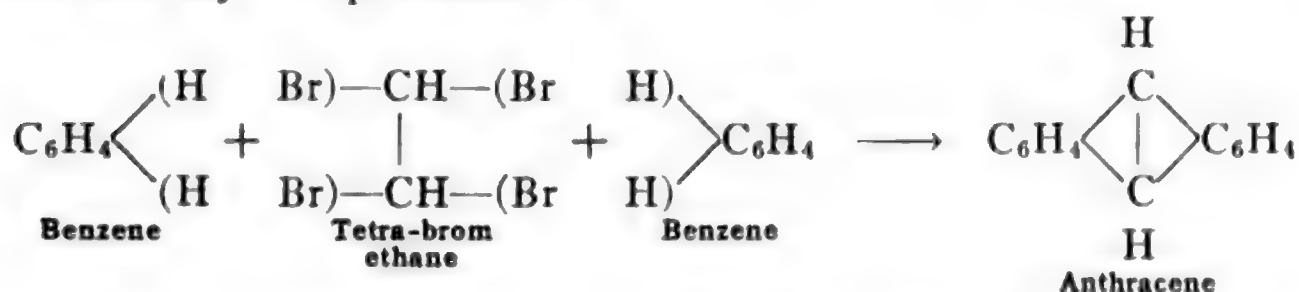
Together with benzene and naphthalene two other hydrocarbons are obtained from coal tar though in much smaller amounts. They are **anthracene** and **phenanthrene**, both of which have the formula $C_{14}H_{10}$. Anthracene together with phenanthrene is present in the coal tar distillate which boils above 270° . The yield of anthracene is about 0.25 to 0.45 per cent of the tar. The crude distillate is purified by a second distillation and separated into two fractions: (1) A product known as 50 *per cent anthracene* which is crystalline and still contains phenanthrene. (2) A less volatile non-crystalline oil known as *anthracene oil*. The 50 per cent anthracene is largely used, just as it is without further purification, in the preparation of **alizarin**, its most important derivative. To obtain pure anthracene from the crude 50 per cent product it is first redistilled after addition of potassium carbonate which forms a non-volatile compound with a constituent known as carbazole.



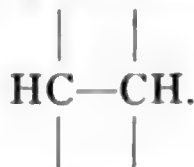
The distillate is then extracted with carbon di-sulphide and sulphuric acid in which the phenanthrene is soluble. The remaining anthracene is now again distilled, recrystallized from benzene and sublimed by means of superheated steam. Pure anthracene crystallizes in colorless shining flakes or scales, m.p. 213° , b.p. 351° . It is soluble in benzene but only slightly in alcohol or ether. In its chemical properties anthracene resembles benzene and naphthalene. It forms addition products with hydrogen or with the halogens which are analogous to those formed from benzene and naphthalene. It readily yields sulphonic acids but does not yield nitro derivatives because it is more easily oxidized by nitric acid than is benzene or naphthalene. When thus oxidized it yields a quinone known as **anthraquinone** analogous to benzoquinone and naphthoquinone.

Condensed Benzene Rings.—That anthracene is a condensed benzene ring compound is proven by several syntheses and reactions.

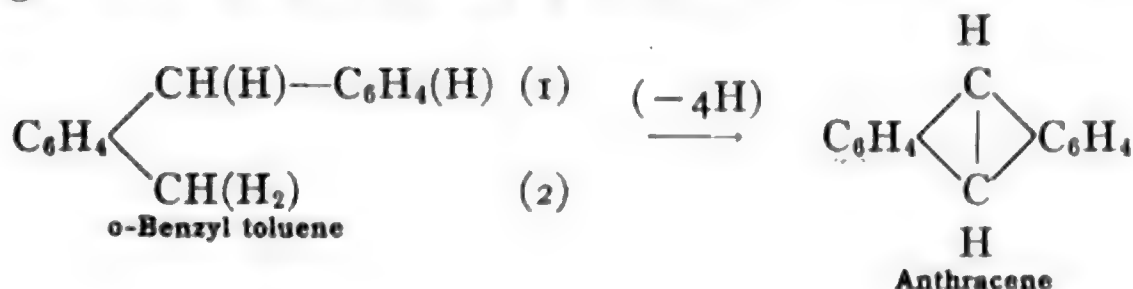
Synthesis from Tetra-brom Ethane.—**Anschtz** showed that in the presence of aluminium chloride *two molecules* of **benzene** condense with *one molecule* of **tetra-brom ethane** and yield **anthracene**. The reaction may be represented as:



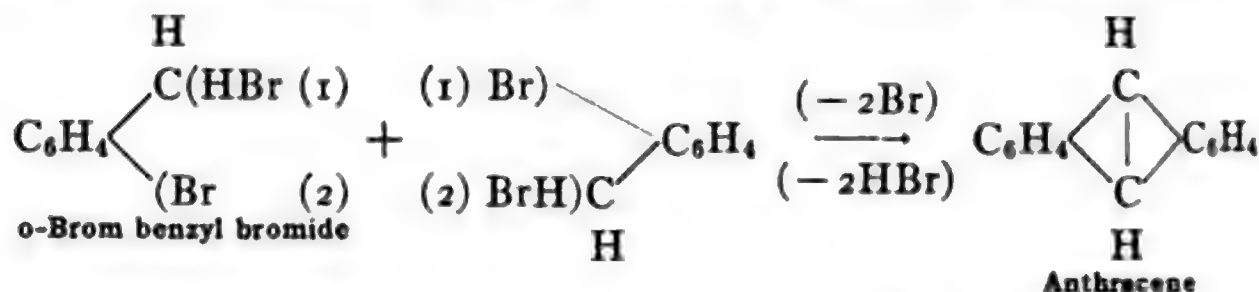
This synthesis indicates that in anthracene there are *two benzene rings* linked together by the *tetra-valent ethane residue*,



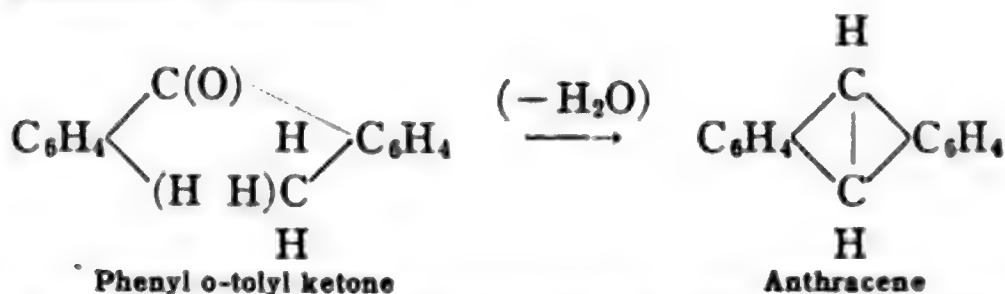
From ortho-Benzyl Toluene.—Such a constitution is supported by other syntheses. When **ortho-benzyl toluene** is heated it loses four hydrogen atoms and **anthracene** is obtained.



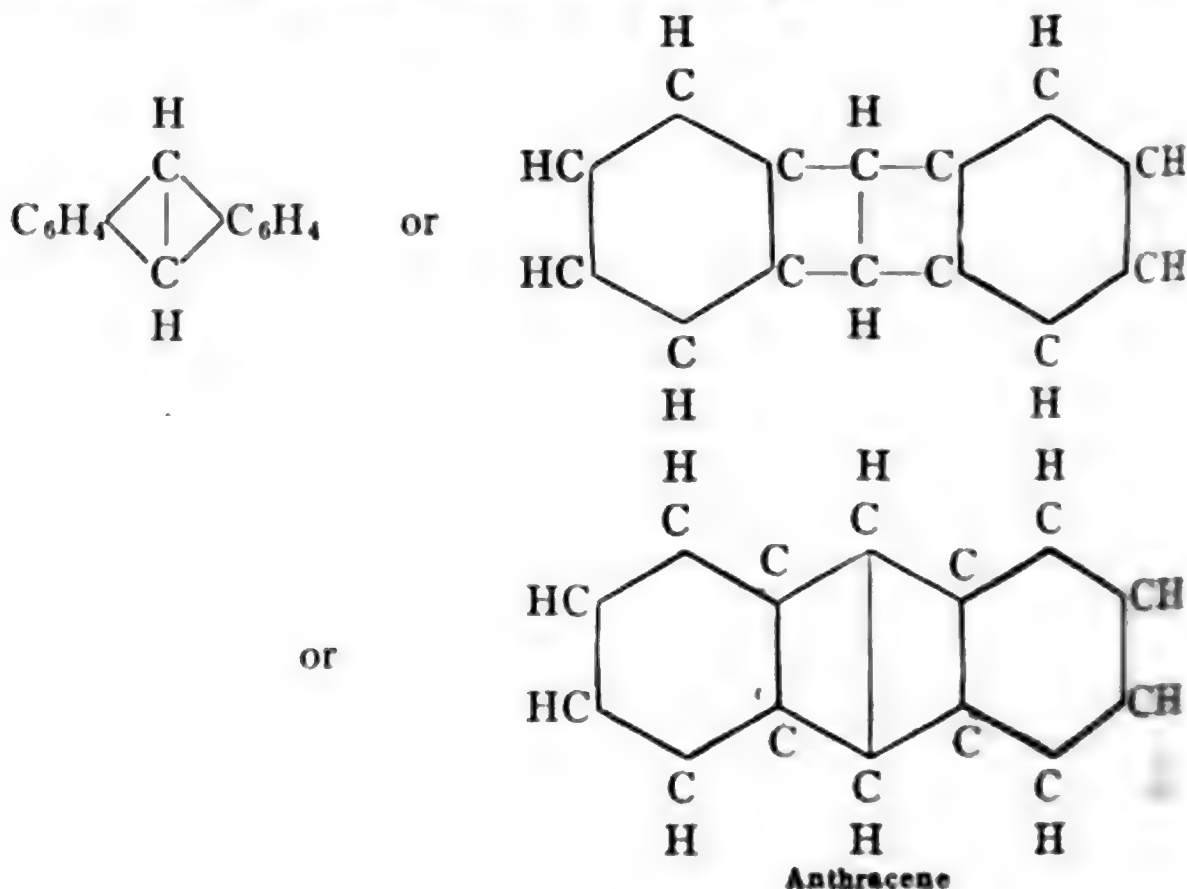
From ortho-Brom Benzyl Bromide.—Also when **ortho-brom benzyl bromide** is heated with sodium, two molecules lose two bromine atoms and two molecules of hydrogen bromide and yield anthracene.



From Phenyl ortho-Tolyl Ketone.—When **phenyl ortho-tolyl ketone**, $\text{C}_6\text{H}_5\text{—CO—C}_6\text{H}_4\text{—CH}_3$, is heated with zinc dust water is lost and anthracene results.



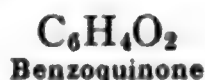
Thus anthracene must be constituted of *two benzene rings each one linked by two ortho positions to an intervening ethane residue*. If such a formula is constructed of tetra-hedral carbons, which will be clear if models are used, we shall have the following:



Three Benzene Nuclei.—Just as naphthalene contains *two* benzene nuclei it will be seen that anthracene similarly contains *three* benzene nuclei. In other words they are condensed benzene ring compounds, the former of *two* and the latter of *three* rings. In naphthalene we have shown that either of the two nuclei may remain as a benzene ring on the destruction of the other. In the case of anthracene we can show with equal proof, as has already been done in the syntheses just given, that the two outside nuclei are true benzene rings. It has never been possible, however, either to start with a benzene ring as the center and build up anthracene by adding on the two outside nuclei or to decompose the compound in such a way that the center nucleus remains as a benzene ring. Nevertheless the evidence is clear that in reality there are three benzene nuclei in the compound, the center nucleus being less strongly aromatic in character due to its condition. Facts bearing on this question are to be found in the study of some of the derivatives of anthracene and these will now be considered.

Anthraquinone

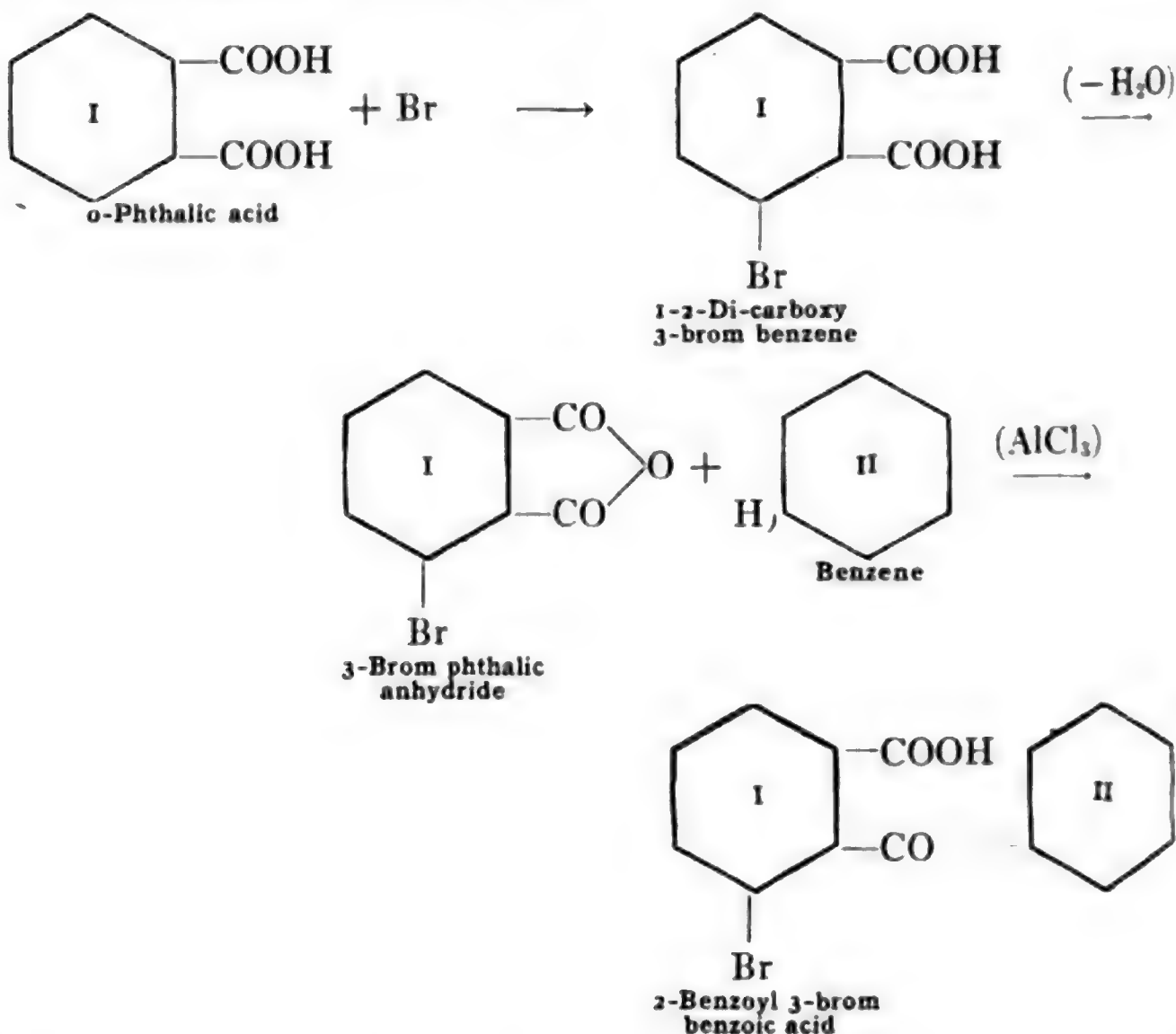
When anthracene is treated with nitric acid instead of yielding nitro substitution products as do benzene and naphthalene it becomes oxidized to a compound known as **anthraquinone**, the composition of which is $C_{14}H_8O_2$ and which may be reduced back to anthracene by heating with zinc dust. The relationship in composition between anthracene and anthraquinone is the same as between benzene and benzoquinone and between naphthalene and naphthoquinone.



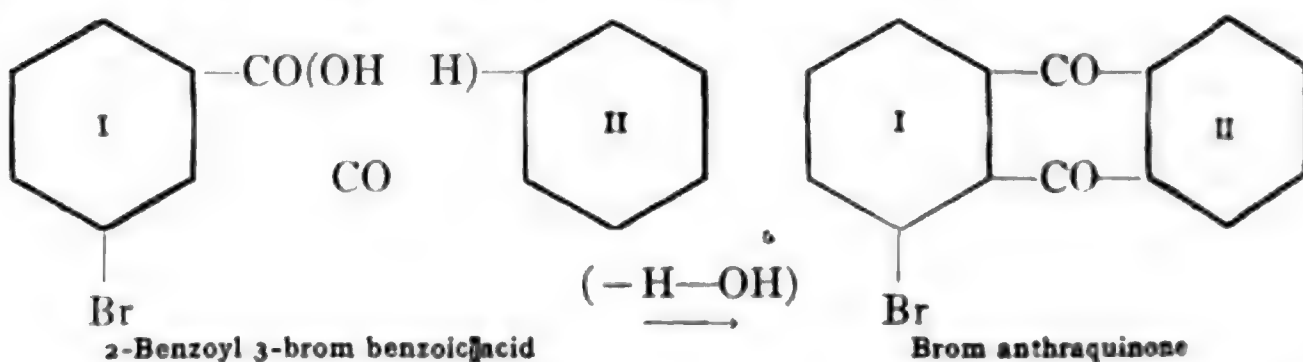
This would indicate a similarity in constitution in these three quinones and this is supported by the following synthesis which also agrees with the constitution of anthracene as already given.

Synthesis from Phthalic Acid.—*ortho*-Phthalic acid yields a monobrom derivative in which the bromine is *ortho* to one carboxyl and *meta* to the other, *i.e.*, **1-2-dicarboxy 3-brom benzene**. This being an *ortho*-phthalic acid yields an anhydride. This anhydride condenses

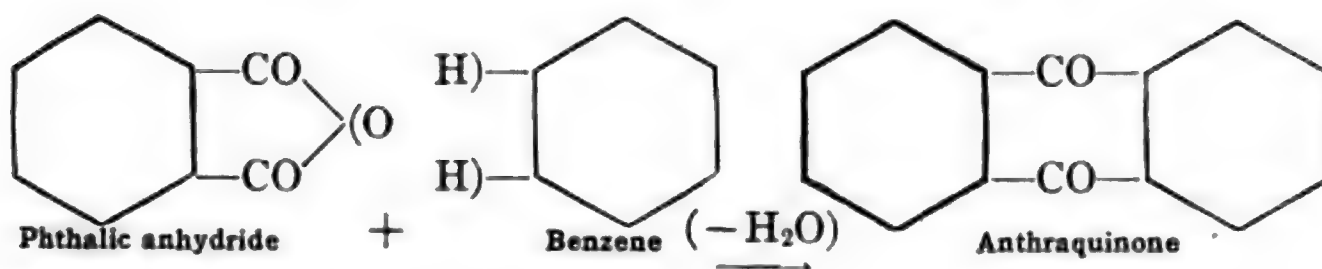
with benzene in the presence of aluminium chloride and the product is **2-benzoyl 3-brom benzoic acid**.



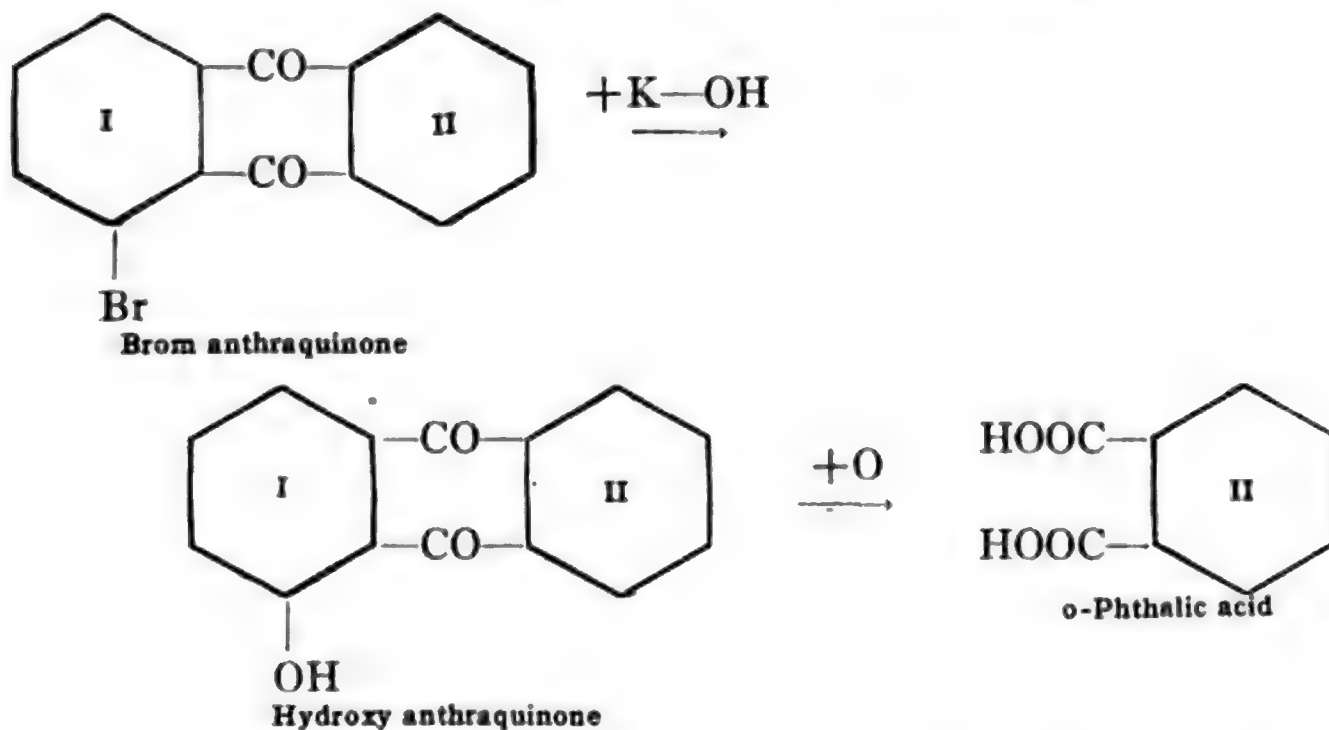
When this **2-benzoyl 3-brom benzoic acid** is heated with sulphuric acid water is lost and **brom anthraquinone** is obtained.



This synthesis is of the same general character as that of anthracene from phenyl *ortho*-tolyl ketone (p. 794). In effect it is the condensation, by the elimination of water, of phthalic anhydride and benzene with the formation of anthraquinone which we may represent as

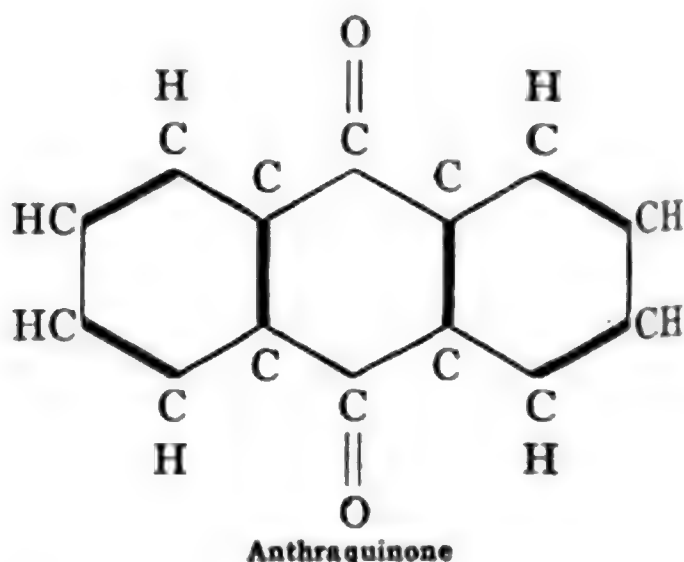
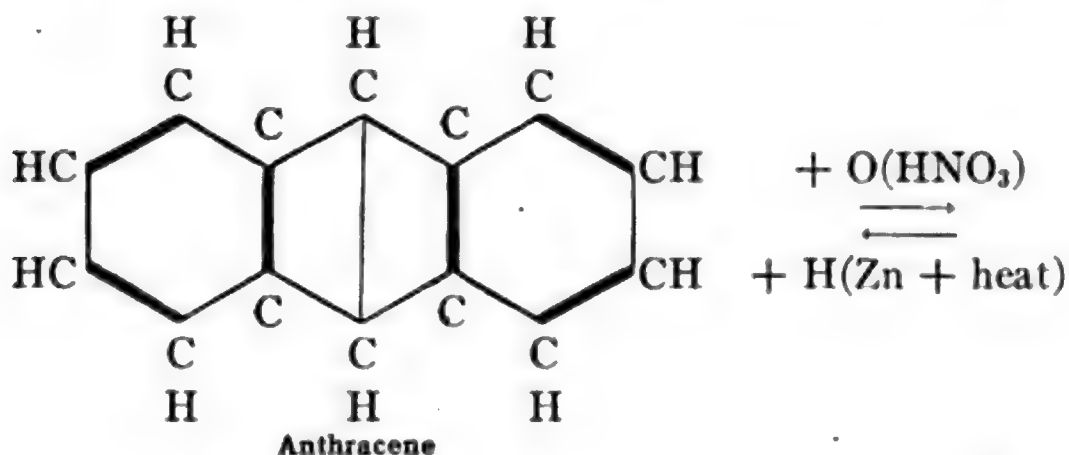


Anthraquinone must therefore have the constitution of two benzene rings linked together by two carbonyl groups. These two carbonyl groups are *ortho* to each other in the ring which was originally *ortho*-phthalic acid. That these carbonyl groups become linked to the second benzene ring in the *ortho* positions also is proven by the conversion of brom anthraquinone into *ortho*-phthalic acid. By means of potassium hydroxide the **brom anthraquinone** is converted into **hydroxy anthraquinone** and this by oxidation yields ***ortho*-phthalic acid**.



In the preceding reactions the benzene nuclei have been numbered I and II in order to follow their course through the various transformations. It may be readily seen, therefore, that the benzene nucleus in brom anthraquinone which remains as a benzene ring in *ortho*-phthalic acid is the nucleus which does not contain bromine. This was derived from the benzene constituent of the synthesis and, in anthraquinone, it is linked to the carbonyl groups by *ortho* positions. Therefore, both benzene nuclei in anthraquinone are linked by *ortho* positions and both are derived from true benzene ring compounds or may remain as benzene rings on the decomposition of the quinone.

The constitutions of anthracene and anthraquinone are thus established as reciprocal oxidation and reduction products. The complete structural formulas may be represented as follows:



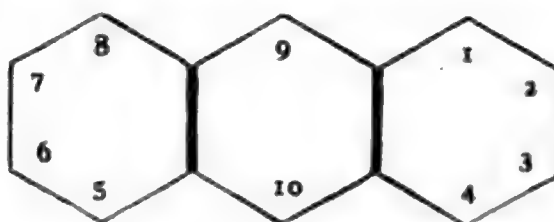
Character of Center Nucleus.—As was stated in connection with anthracene itself we can not say positively as to the character of the center nucleus in either the hydrocarbon or the quinone. In anthracene the aliphatic character of this center nucleus is indicated by its formation from an ethane residue, by the tetra-brom ethane synthesis. This does not, however, preclude the possibility of its becoming a true benzene nucleus when condensed with two benzene rings, for benzene itself may be made from aliphatic hydrocarbons, from acetylene by polymerization (p. 478), and from hexane through hexa-methylene with the loss of hydrogen after the formation of the cyclo-paraffin (p. 469). Also naphthalene, in which there is no doubt of the benzene character of the two nuclei, may have one nucleus formed from an aliphatic chain as in the syntheses given (p. 767) from phenyl butylene bromide, from phenyl vinyl acetic acid and from tetra-carboxy ethane. In the same way the facts in regard to anthraquinone do not prove

that the center nucleus is not of benzene character. Anthraquinone lacks distinctive quinone character. It is not colored, has no strong odor and is not volatile with steam. On the other hand, it resembles ketones being like benzophenone, di-phenyl ketone. In fact its structure is clearly that of a *di-phenyl di-ketone*. The progressive loss of quinone character from benzoquinone, to naphthoquinone, to anthraquinone, and the relation of these quinones to their corresponding hydrocarbons, is very interesting and instructive. The single benzene ring of benzene itself can not be directly oxidized to the quinone and the quinone when obtained has very distinctive characters. These characters are distinct from those of ketones though the structure of benzoquinone is probably that of a di-ketone (p. 636). Naphthalene' on the other hand, consisting of two benzene nuclei is able to be oxidized directly to naphthoquinone by means of chromic acid. Here the benzene nucleus which yields the quinone group is not in itself a complete benzene ring as it possesses only four out of six carbons independent of the other nucleus. It must, therefore, be less strongly benzene in its character, yet it may become a complete ring on the destruction of the other nucleus. The character of naphthoquinone is also less strongly quinone-like and more like a ketone. Now in anthracene the center nucleus which yields the quinone group is still less a complete benzene ring in itself, as it possesses only two carbons independent of the other two nuclei. It is thus even less strongly benzene in character than either nucleus in naphthalene and in fact has never been retained as a complete ring by the destruction of the other two nuclei. Anthracene, therefore, is able to have this center nucleus oxidized to the quinone group more easily than in the case of naphthalene, for anthraquinone is obtained by simply oxidizing the hydrocarbon with nitric acid. Also, the quinone character of anthraquinone is still less than of naphthoquinone and it is much more like a ketone.

That the center nucleus in anthracene and anthraquinone is in reality a true benzene nucleus is supported simply by the structural and space relations of the constituent carbon atoms which according to the tetra-hedral theory are exactly the same as in benzene, in the two nuclei of naphthalene, or the other two nuclei of anthracene itself. For all of these nuclei the true benzene character is fully proven. Thus while it is best not to place too much emphasis upon the three

benzene nuclei structure of anthracene and anthraquinone there seems to be no real reason for not accepting it, as it is not contrary to the evidence derived from either the syntheses of the compounds or their properties and it is in accord with the tetra-hedral theory of carbon and its application to the benzene ring.

Isomerism.—An examination of the formula for anthracene will show that the number of isomeric substitution products may be greater in number than in the case of naphthalene. The facts in regard to the mono- and di-substitution products are that there are *three mono-substitution products* and *fifteen di-substitution products* with like substituents. Numbering the positions in the anthracene formula we have:



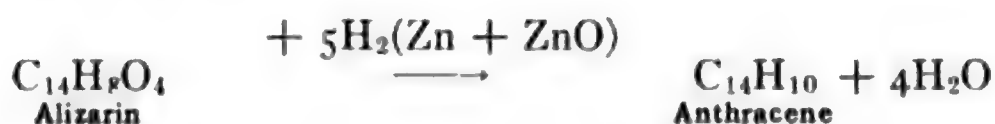
The mono-substitution product with the substituent in positions 1, 4, 5 or 8, is named *alpha*; in positions 2, 3, 6 or 7, *beta*; and in position 9 or 10, *gamma*. If two substituents are alike the following fifteen isomeric di-substitution products are possible: 1-2, 1-3, 1-4, 1-5, 1-6, 1-7, 1-8, 1-9, 1-10, 2-3, 2-6, 2-7, 2-9, 2-10, 9-10. Of the derivatives of anthracene a large number are known but only two will be taken up in detail, viz., **anthraquinone**, which we have already considered, and **alizarin**.

Alizarin

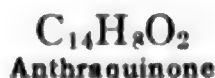
Turkey Red.—**Alizarin** is the chief constituent of the coloring matter **Turkey red**, which has been known since ancient times and which was obtained from the root of the **madder plant**, *Rubia tinctorum* L. The substance is of special interest because the determination of its constitution was one of the early triumphs of organic chemistry and because it was the first natural dye to be synthetically prepared. The name is derived from the oriental name for the madder, viz., *alizari*. In the madder root it is present as a glucoside known as **ruberythric acid**, which, on hydrolysis by fermentation or by boiling with acids, yields **glucose** and **alizarin**. Alizarin is a solid which sublimes as orange red needles, m.p. 289° , insoluble in water but slightly soluble in alcohol.

Synthesis, Graebe and Liebermann.—The determination the of constitution of alizarin and its synthetic preparation are both due largely to the work of Graebe and Liebermann in 1868.

Reduction to Anthracene.—They first obtained the hydrocarbon mother substance which they proved to be **anthracene**, and which was obtained on reducing alizarin by dry distillation with zinc dust. This method of reduction was discovered by Baeyer and has been referred to before as being applicable to the conversion of anthraquinone into anthracene (p. 795). The action is due to the presence of zinc oxide in the zinc dust. Alizarin has the composition $C_{14}H_8O_4$. Therefore the empirical reaction is

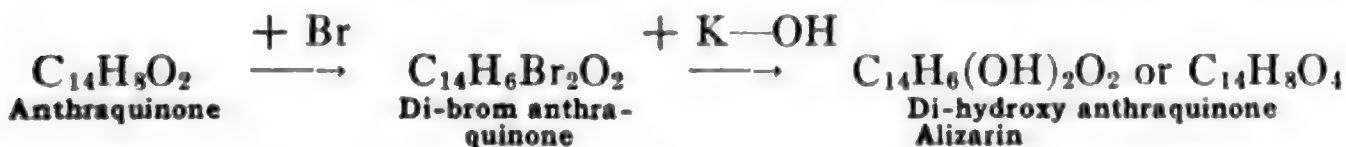


The relationship in composition between anthracene, anthraquinone and alizarin, viz.,

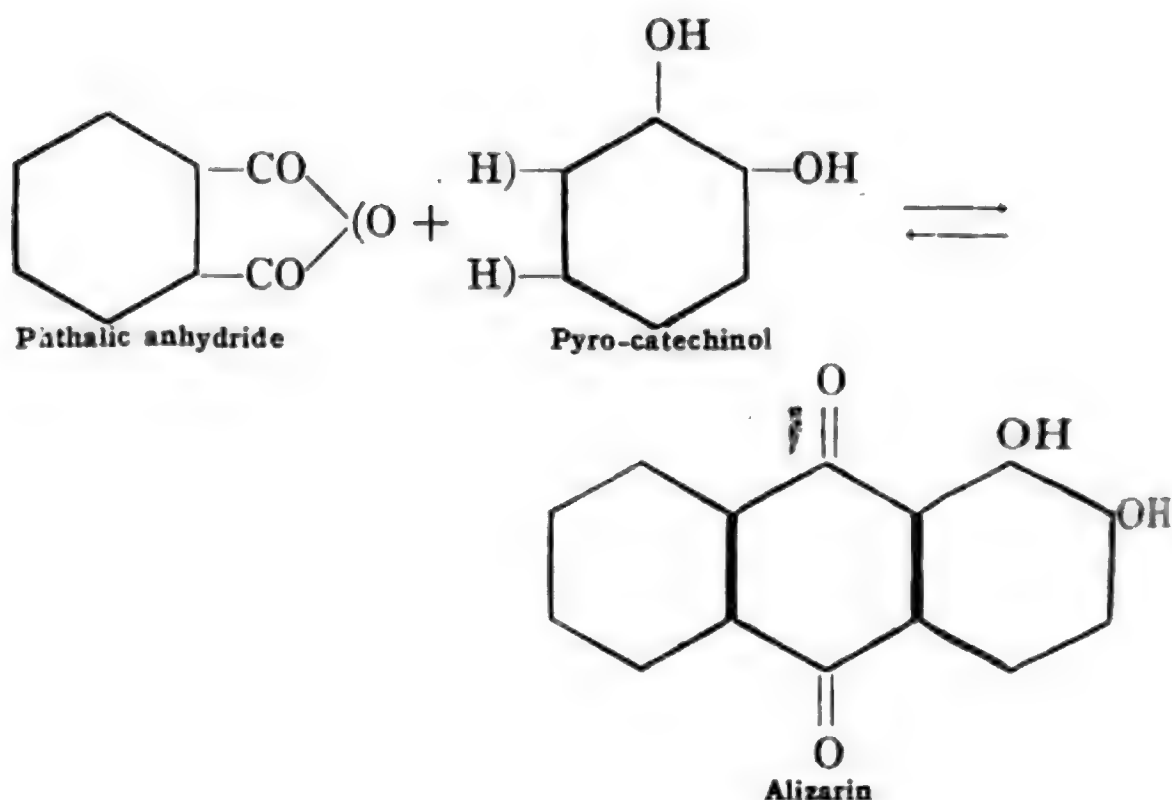


led them to believe that anthraquinone was an intermediate product and that alizarin might be di-hydroxy anthraquinone.

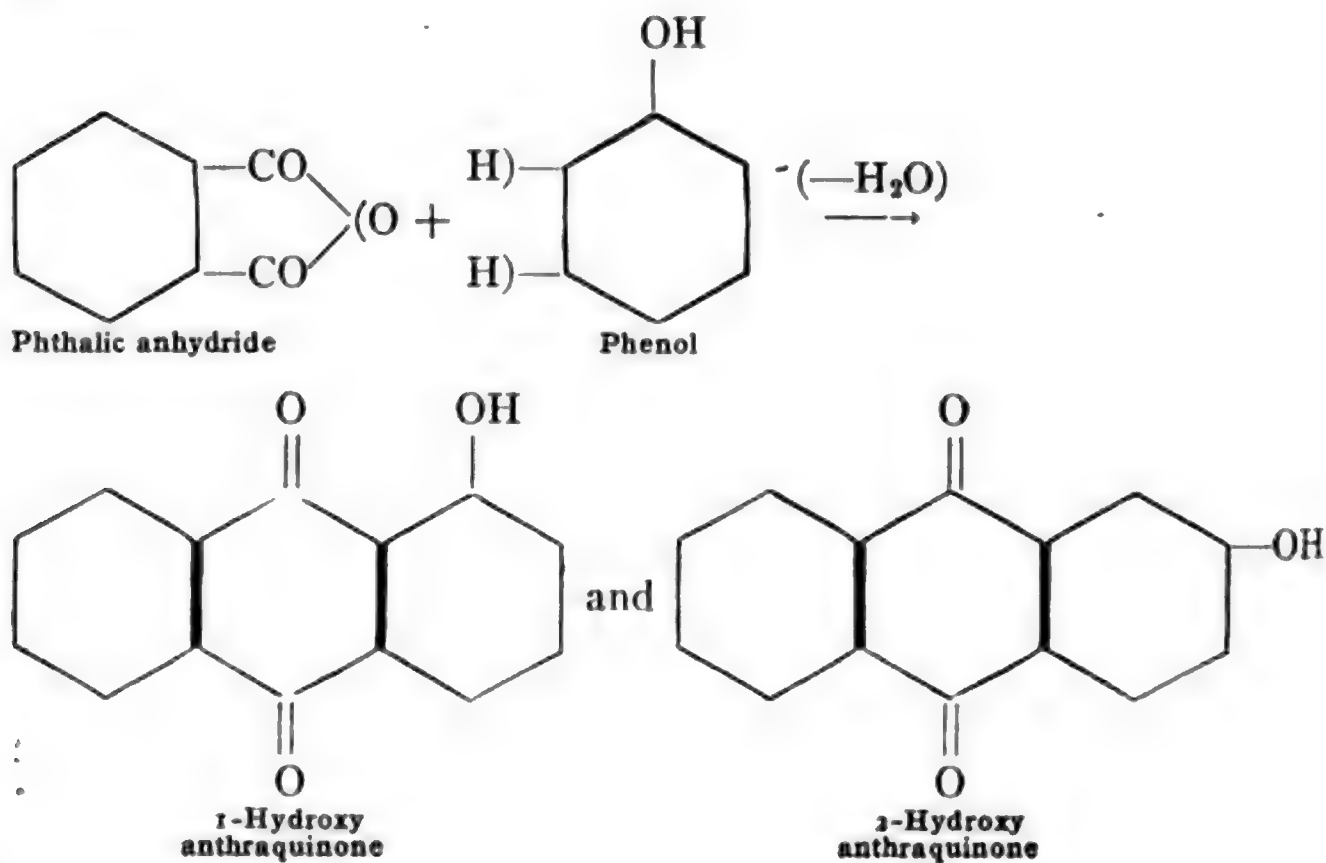
1-2-Di-hydroxy Anthraquinone, Baeyer and Caro.—To test this point they prepared a **di-brom anthraquinone** and fused it with potassium hydroxide. The product proved to be **alizarin**, thus establishing it as **di-hydroxy anthraquinone**.



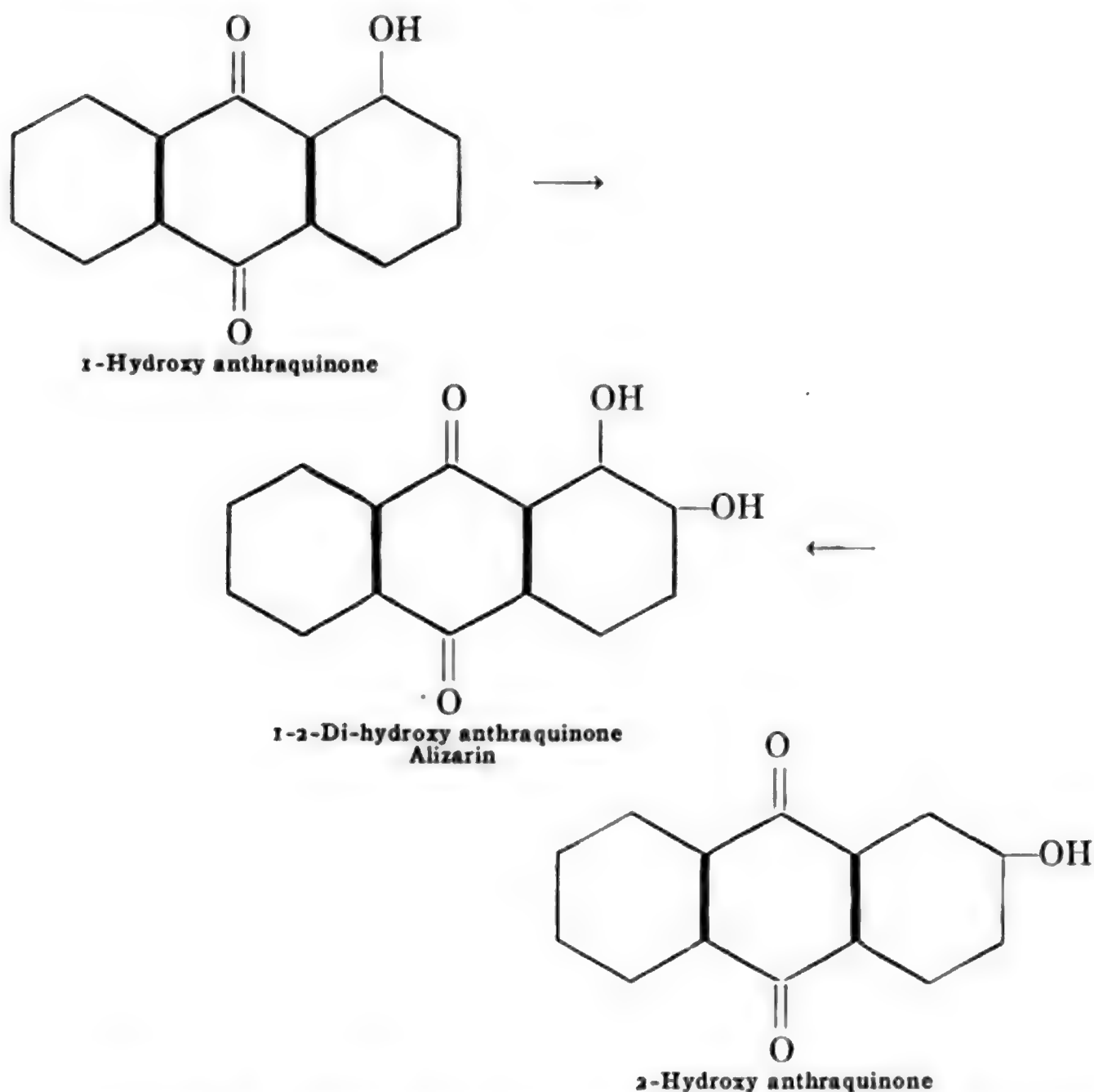
The remarkable thing is, that while there are *ten* possible di-brom or di-hydroxy anthraquinones, the particular one necessary was obtained by Graebe and Liebermann. The positions of the two hydroxyl groups were determined by Baeyer and Caro. When alizarin is heated **pyrocatechinol**, **1-2-di-hydroxy benzene**, is obtained. Also when pyrocatechinol is heated with *ortho*-phthalic acid and sulphuric acid alizarin results. This last synthesis is analogous to that of anthraquinone from benzene and *ortho*-phthalic acid (p. 796).



This relationship of alizarin to pyro-catechinol proves that the two hydroxyl groups must be *ortho* to each other, but this condition is possible if the hydroxyls are either 1-2 or 2-3. **Baeyer and Caro** established the positions as 1-2 as follows. When **phenol** is heated with **ortho-phthalic acid** and sulphuric acid *two mono-hydroxy anthraquinones* are obtained.

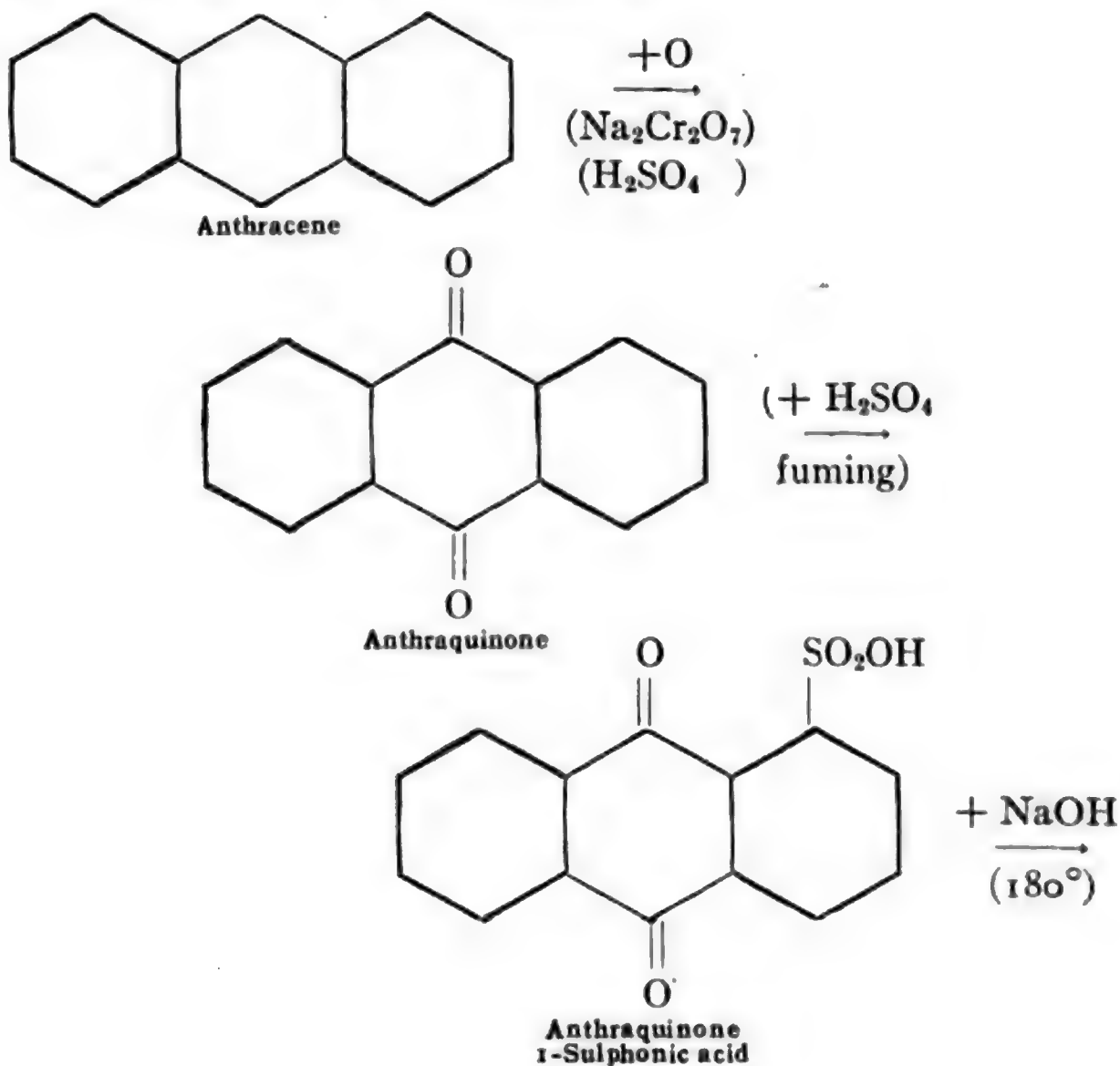


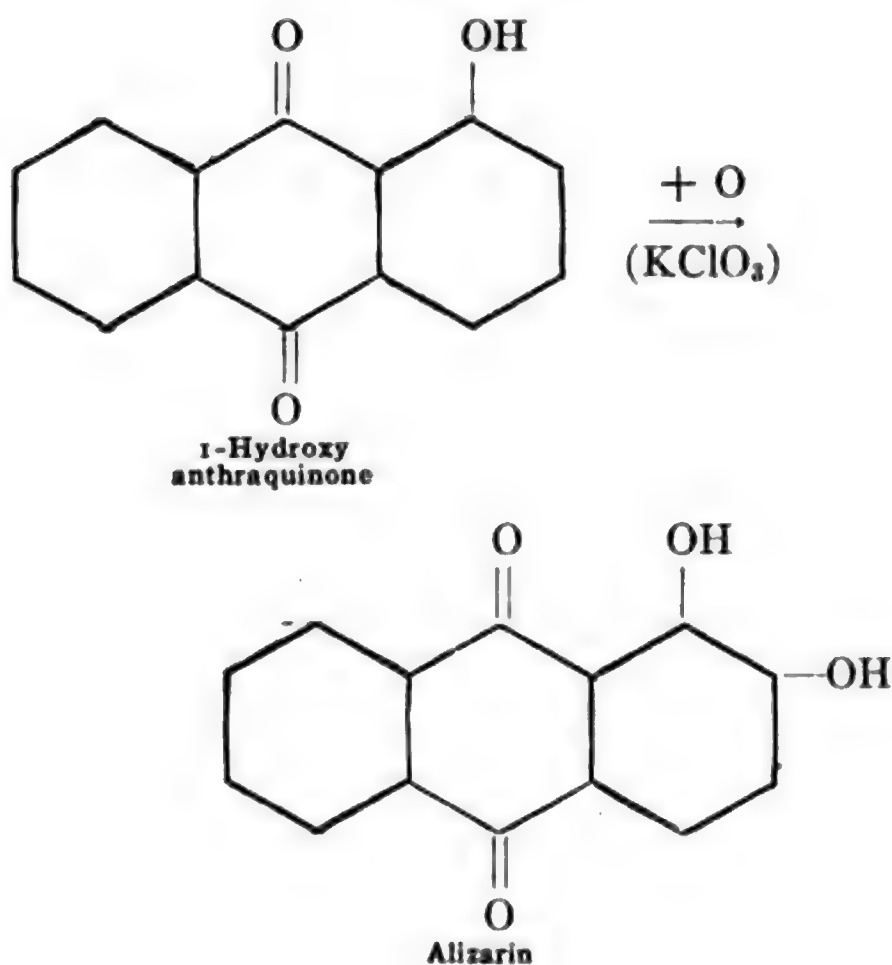
As will be seen, only these two mono-hydroxy compounds are possible. Now both of these mono-hydroxy anthraquinones yield alizarin by the introduction of a second hydroxyl group. The only constitution possible for a di-hydroxy anthraquinone obtained from both of these two mono-hydroxy anthraquinones is the 1-2-*di-hydroxy* compound. As alizarin is thus obtained the two hydroxyl groups in it must be in the 1-2 positions and not in the 2-3 positions.



Commercial Synthesis.—In their work Graebe and Liebermann used a second synthesis for preparing alizarin. When **anthraquinone mono-sulphonic acid** is fused with potassium or sodium hydroxide alizarin is obtained. In this synthesis the alkali fusion replaces the sulphonic acid group with hydroxyl and at the same time oxidizes the

neighboring hydrogen to hydroxyl. A modification of this synthesis is the commercial process for making alizarin today. Crude anthracene, known as 50 *per cent anthracene* (p. 792), is converted into crude anthraquinone by oxidation with sodium bichromate, $\text{Na}_2\text{Cr}_2\text{O}_7$, and sulphuric acid. The crude anthraquinone is then heated with ordinary sulphuric acid to 100° . This treatment sulphonates the impurities present, and allows their removal from the non-sulphonated anthraquinone. The thus purified anthraquinone is then sulphonated by heating to 160° with 50 per cent fuming sulphuric acid. The product is largely **anthraquinone 1-sulphonic acid**. Instead of fusing this with alkali alone the sodium salt of the sulphonic acid is treated with a mixture of sodium hydroxide and potassium chlorate and heated in an autoclave to 180° for 48 hours. The potassium chlorate is a more active oxidizer than the alkali alone, the product of the combined alkali fusion and oxidation being, as in **Graebe and Liebermann's** original synthesis, **alizarin**. The reactions are:





In this synthesis it is interesting that it is the mono-sulphonic acid of anthraquinone and not the di-sulphonic acid which is the intermediate product. Other syntheses have been used commercially. Anthraquinone may be converted into alizarin without sulphonation by treating it with a mixture of sodium hydroxide, potassium hydroxide and sodium chlorate and heating to 200° . Also electrolytically by passing a current through a mixture of anthraquinone and fused potassium hydroxide.

Industrial Importance.—The synthesis of alizarin by **Graebe** and **Liebermann** was the first case of a common natural dye being prepared in the laboratory. As the synthesis starts with anthracene, a substance obtained in good yields from coal tar, it affords at once a cheap commercial source for the *synthetic preparation of a natural product*. Hardly any synthesis that has been worked out in the laboratory has had such an immediate effect upon industry as this one, and in addition to this it exerted a strong influence upon similar syntheses of other dyes. In 1868 Turkey red was a very common and valuable dye and the growth of the madder plant, in France especially, was an important industry. In their original paper **Graebe** and **Liebermann** make this statement:

"We need not indicate the importance of our discovery to the madder industry if it is possible to make it a technical success." That their synthesis was a success may be seen from a few facts. In 1868 France produced about 250,000 tons of madder, exporting over \$5,000,000 worth of products. In three years the exportation fell to about \$800,000 and before a decade had passed the growth of madder had practically ceased. A common saying in the madder country, as given by **Schorlemmer** is: "it is no longer grown as it is now made by machinery." When we consider later the synthetic preparation of indigo we shall find that a similar result was effected.

The use of alizarin as a dye depends upon the fact that with mordants of metallic oxides it forms insoluble lakes which are deposited on the fibers of the cloth and thus dye it. These lakes are of different colors depending upon the metallic salt used. Aluminium gives a *red* color known as *Turkey red*. Ferrous iron gives *black-violet* and ferric iron a *brown-black*. Tin produces a *red-violet* color as stannous salts and a *violet* as stannic. Chromium salts give a *brown-violet* color.

Nitro, amino and sulphonic acid derivatives of alizarin are also dyes of various colors and are known as **alizarin orange**, **alizarin maroon**, **alizarin red**, etc. Also there is present in the madder root another dye compound known as **purpurin** which is **1-2-4-tri-hydroxy anthraquinone**. Isomeric tri-hydroxy anthraquinones are dyes also but it is interesting that in all of these poly-hydroxy anthraquinones which are dyes two of the hydroxyls are always in the 1-2 positions.

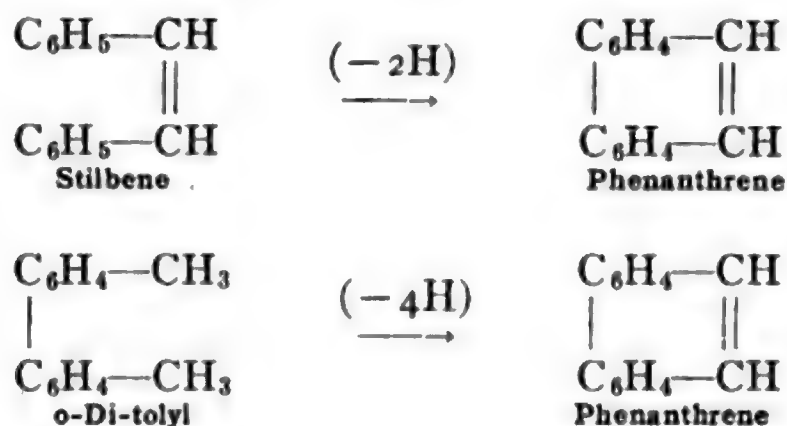
PHENANTHRENE AND DERIVATIVES

Phenanthrene

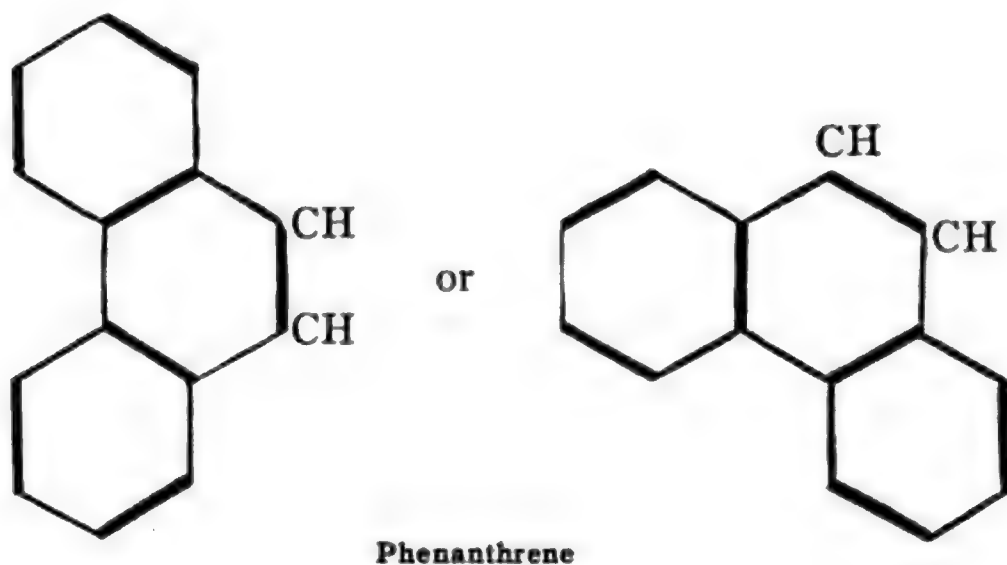
The third hydrocarbon consisting of condensed benzene nuclei similar to naphthalene and anthracene is known as **phenanthrene**. It has the composition $C_{14}H_{10}$ and is thus isomeric with anthracene. It is found associated with the latter in the coal tar distillate boiling above 270° and is separated by solution in carbon disulphide (p. 793). It is a solid crystallizing in colorless flakes, m.p. 99° , b.p. 340° . It is only slightly soluble in water, a little more soluble in alcohol and soluble in ether.

Synthesis from Stilbene and Di-tolyl.—Two similar syntheses indicate the constitution of phenanthrene. When **stilbene**, (p. 762),

$\text{C}_6\text{H}_5\text{—CH=CH—C}_6\text{H}_5$ is heated it loses two hydrogens and **phenanthrene** results. Also **ortho-di-tolyl**, $\text{CH}_3\text{—C}_6\text{H}_4\text{—C}_6\text{H}_4\text{—CH}_3$, when heated loses four hydrogens and yields **phenanthrene**. These reactions yielding the same product must necessarily be represented as follows:

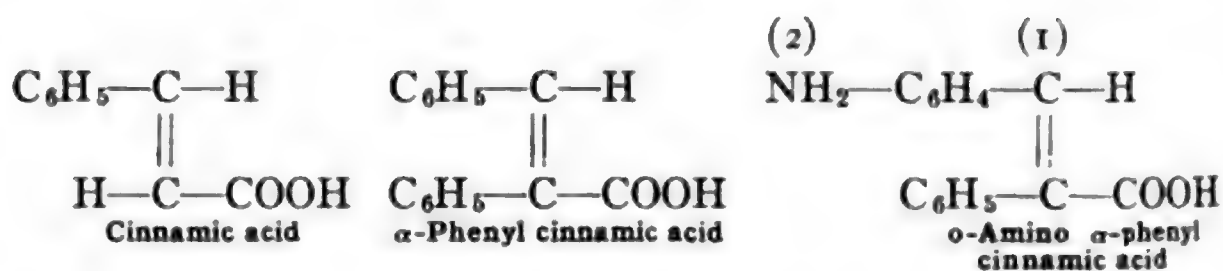


Expressing a compound of this constitution by means of benzene rings we have:

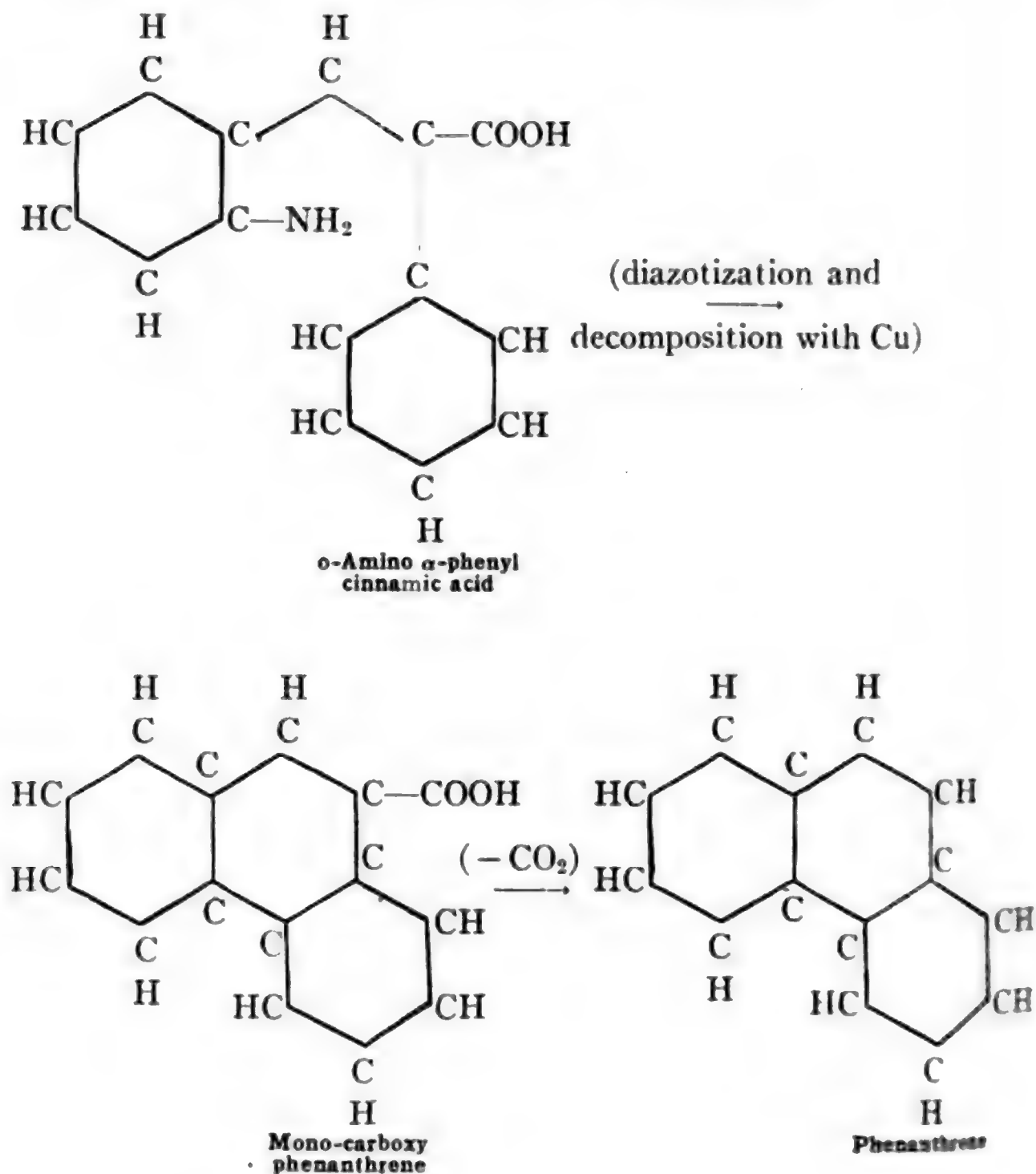


Such a formula represents a compound consisting of three condensed benzene nuclei. More conclusive proof of the constitution is afforded by other syntheses and by the decomposition of the hydrocarbon.

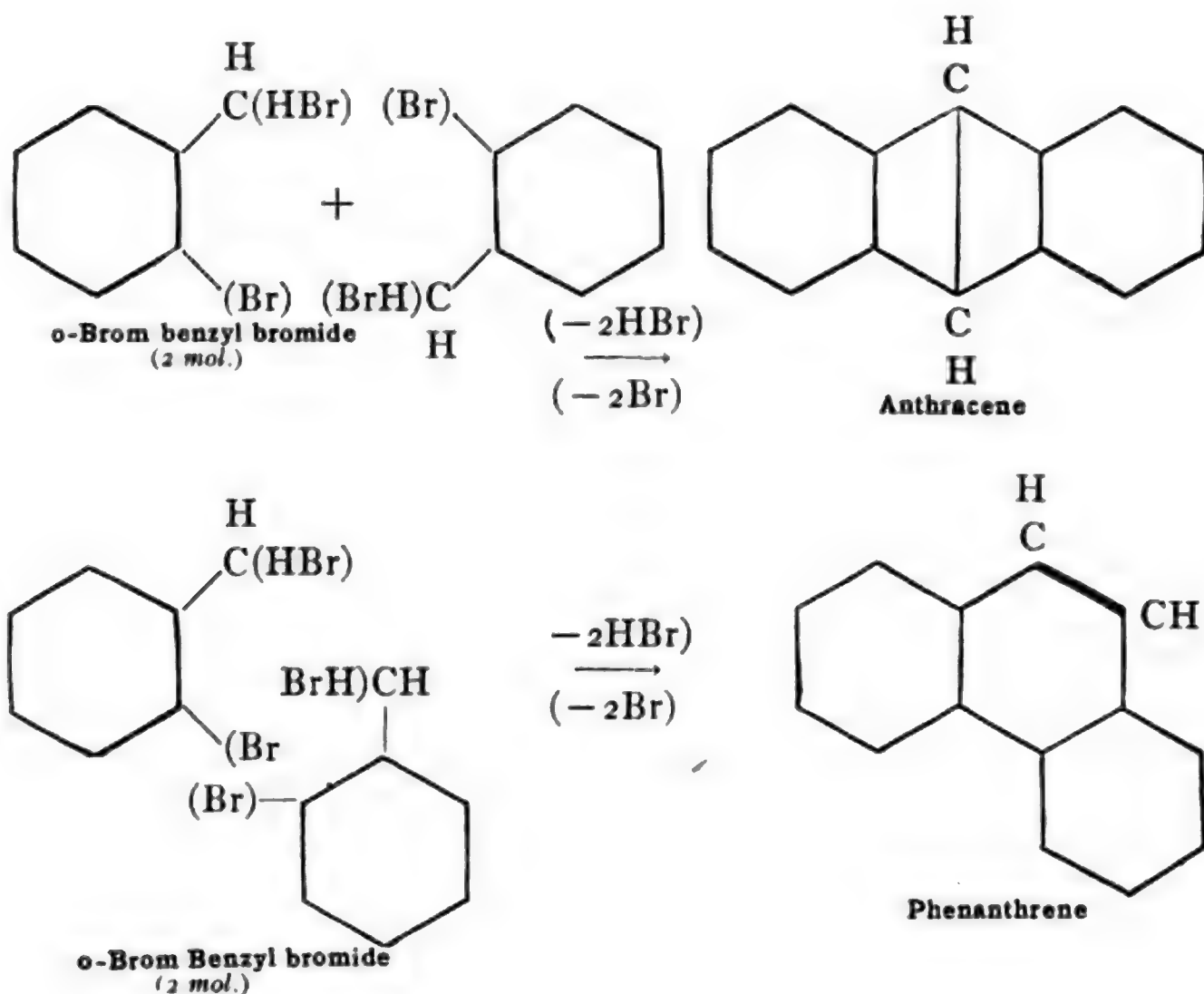
From ortho-Amino alpha-Phenyl Cinnamic Acid.—Referring to cinnamic acid (p. 697) the constitution of **ortho-amino alpha-phenyl cinnamic acid** will be as shown by the following relationships.



When this amino derivative is diazotized and decomposed in the presence of metallic copper (**Sandmeyer reaction**) the two benzene rings become linked together yielding a *mono-carboxy acid* of phenanthrene and this by loss of carbon dioxide yields **phenanthrene**.

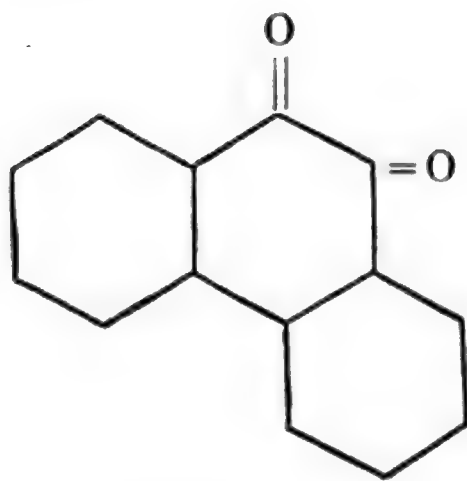


From ortho-Brom Benzyl Bromide.—From this constitution for phenanthrene and its similarity to the constitution of anthracene, both being made up of three benzene nuclei, it will not be surprising that the same synthesis will yield the two compounds. This is the synthesis from **ortho-brom benzyl bromide** (p. 794), which by the loss of two molecules of hydrobromic acid and two atoms of bromine, by heating with alkali, yields both compounds.

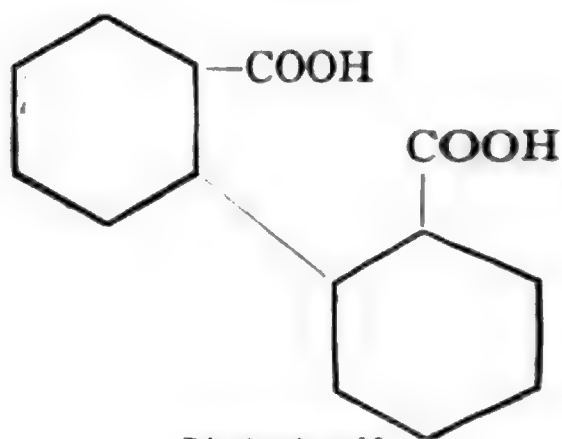


The different manner in which the loss of bromine and hydrogen occurs is plainly shown and the two hydrocarbons being isomeric compounds the difference in constitution is apparent.

Phenanthraquinone, Di-phenic Acid.—Two derivatives of phenanthrene may be simply mentioned. On oxidation with chromic acid phenanthrene yields a quinone known as **phenanthraquinone**. By further oxidation the intermediate benzene nucleus breaks and a di-carboxy acid known as **di-phenic acid** is obtained (p. 733).



Phenanthraquinone



Di-phenic acid

Retene, Pyrene.—Other condensed benzene nuclei compounds are known. **Pyrene** is a four benzene nuclei compound and **retene** is a condensed ring compound found in pine tar.

4. HYDROGENATED BENZENE COMPOUNDS

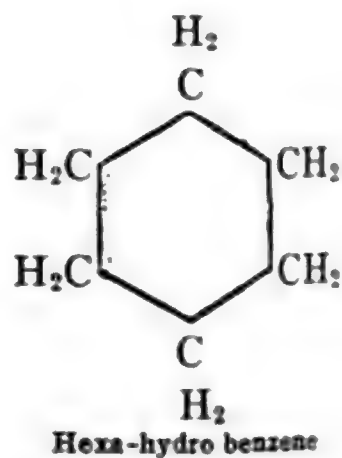
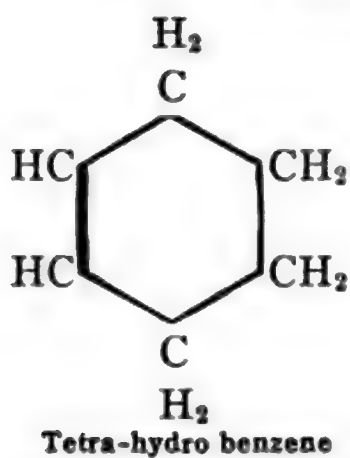
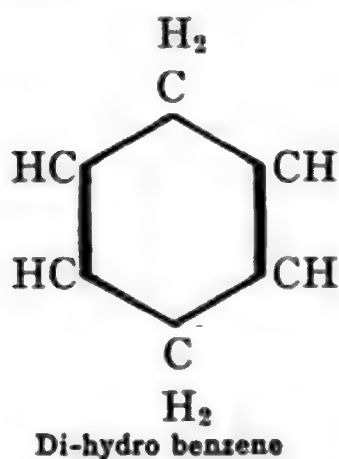
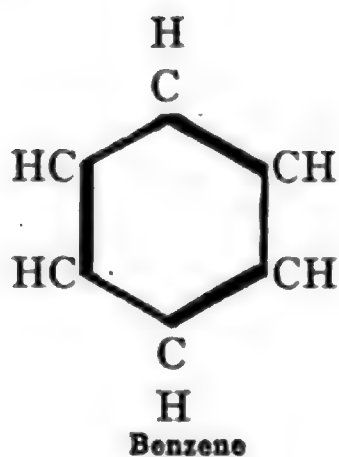
One more class of hydrocarbons is yet to be considered which includes compounds more closely related to benzene and its homologues than to any of the poly-ring or condensed ring hydrocarbons such as di-phenyl, naphthalene or anthracene. The hydrocarbons to be studied now are of two groups known as *naphthenes* and *terpenes*. From the terpenes a very important series of derivatives is obtained which includes the common substance known as **camphor**. Also we shall consider the group of substances known as *essential oils*, such as *oils of turpentine, clove, lemon, geranium*, etc., many of which are terpenes. Finally the interesting and valuable product **rubber** or **caoutchouc** is also a terpene.

NAPHTHENES

The petroleum oil which is found in the Caucasus in the region of the Black Sea and commonly known as *Russian petroleum* differs from American petroleum in that while the latter contains almost entirely hydrocarbons of the aliphatic series, the former contains hydrocarbons known as *naphthenes* which are *hydrogenated benzene compounds*.

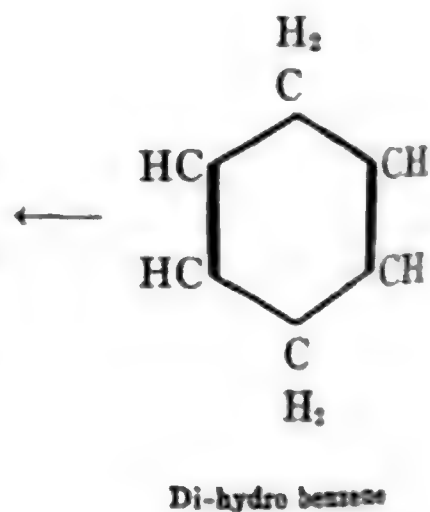
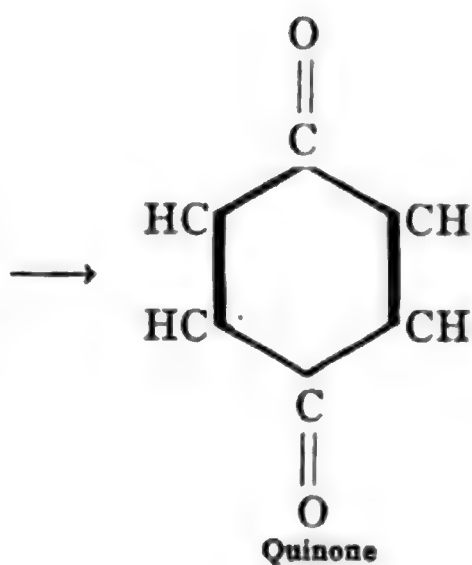
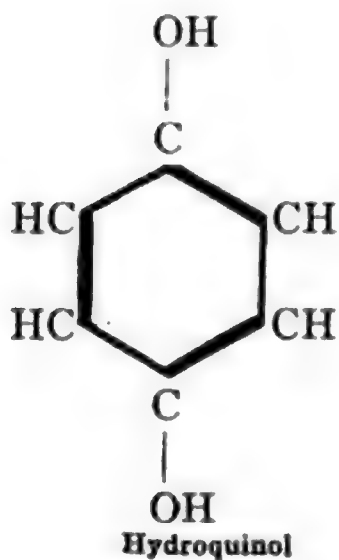
Hydro Benzenes.—In discussing the constitution of benzene (p. 468) it was shown that by the addition of six hydrogen atoms to the benzene molecule it was converted into **cyclo-hexane** or **hexa-hydro benzene**. The addition of hydrogen according to the above reaction takes place when benzene and hydrogen are passed over finely divided nickel, **Sabatier and Senderens reaction**. Intermediate between benzene and hexa-hydro benzene we have partially hydrogenated products resulting from the addition of *two* or *four* hydrogen atoms per molecule of benzene. These hydro-benzenes are the **naphthenes**. They are also known as *hydro-aromatic compounds*.

The series is as follows:

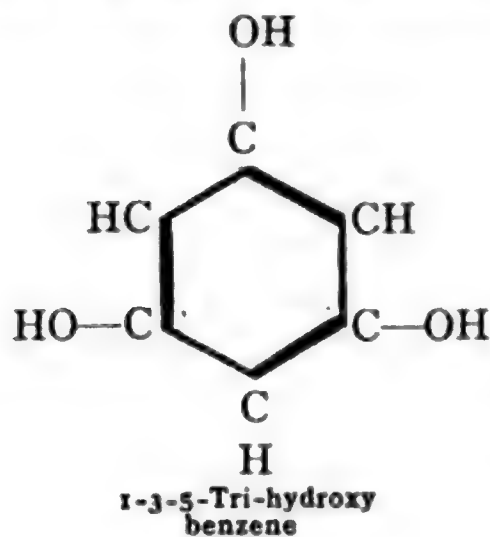


These naphthene hydrocarbons are the mother substances of important derivatives some of which have already been considered as direct derivatives of benzene but which may also be regarded as derivatives of the naphthenes.

Quinone and Phloroglucinol.—**Benzoquinone** or **quinone** (p. 636) is considered a *di-ketone* derivative of benzene because of its relation to **hydroquinol** or **para-di-hydroxy benzene**. It may also be considered as an *oxygen derivative* of **di-hydro benzene**.

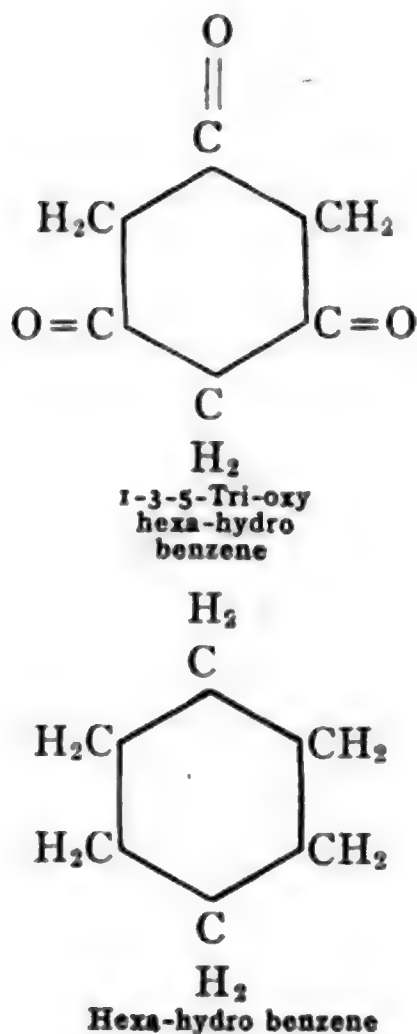


Also **phloroglucinol** the **1-3-5-tri-hydroxy benzene** may have the tautomeric constitution of a *tri-ketone* (p. 621) in which case it is a *tri-oxy derivative* of **hexa-hydro benenze**.



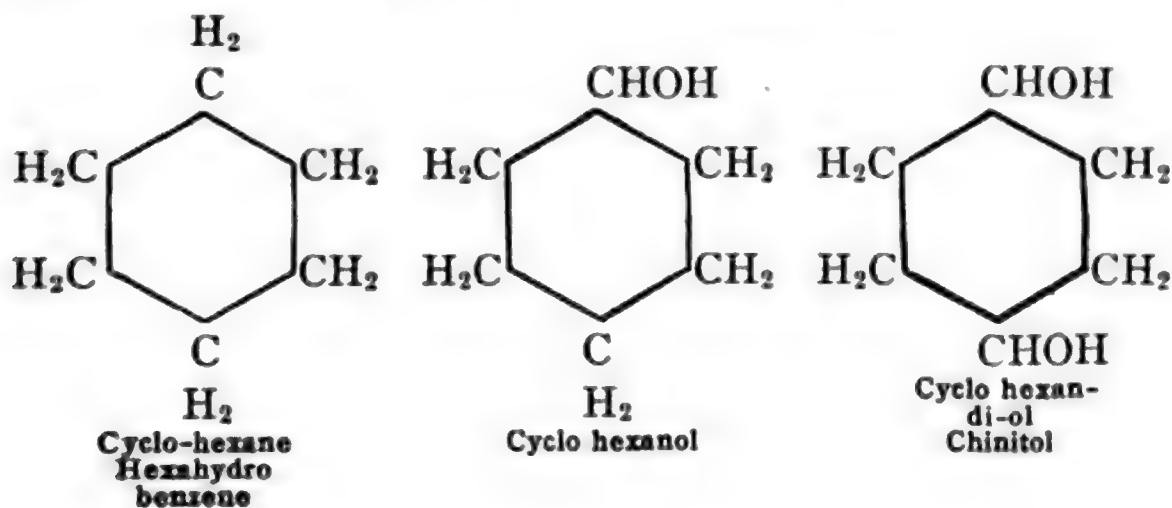
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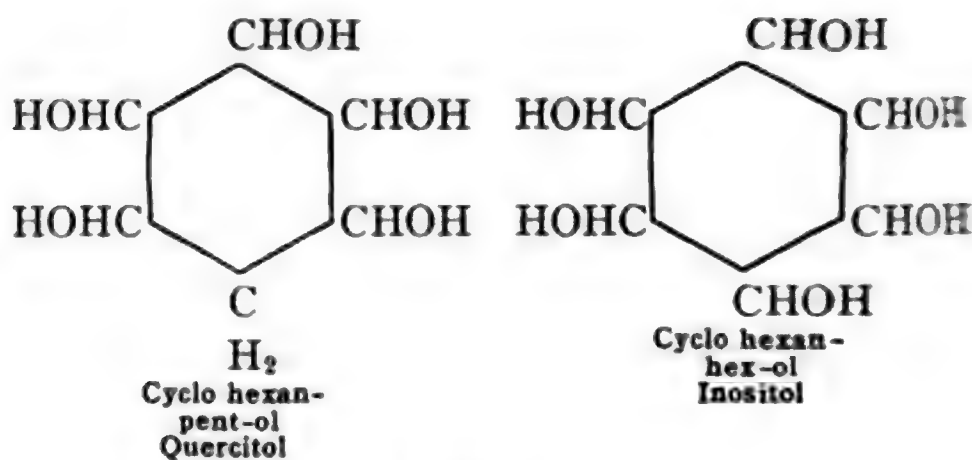
Phloroglucinol



CYCLO HEXANOLS

A less complete oxidation of hexa-hydro benzene than that represented by the relationship of the tri-ketone compound above yields a series of cyclic secondary alcohols some of which are natural substances. Their relationship to hexa-hydro benzene is as follows:





Chinitol, Quercitol, Inositol

The last three compounds, the two, five and six hydroxyl derivatives of hexa-hydro benzene, are natural substances known as **chinitol**, **quercitol** or *acorn sugar* found in acorns, and **inositol** or *muscle sugar* found in animal muscle tissue. These compounds are all sweet in taste and were at one time supposed to be true sugars. This was indicated also by the fact that the last is isomeric with **glucose**, its composition being $\text{C}_6\text{H}_{12}\text{O}_6$. However, the compound is *not* fermented by yeast zymase, it does *not* reduce Fehling's solution and does *not* react with phenyl hydrazine. It is therefore *not a true sugar*. Its relation to benzene is shown also by the fact that on reduction with hydriodic acid it yields **phenol** and **benzene**. Inositol is known as muscle sugar because of its sweet taste and because it is found in animal muscle tissue, especially in the heart and brain. It is also found in various leaves, roots and seeds, such as peas, beans and cereals.

Phytin.—In the latter it is present in combination as a substance known as **phytin**. This substance is a calcium or magnesium salt of a *hexa-phosphoric acid ester* of **inositol**. It is the compound in which most of the phosphorus present in seeds is contained.

TERPENES

Strictly speaking the terpenes are hydrocarbons which are present in, or are obtained by steam distillation from, certain natural products, such as **camphor** and *oil of turpentine*; certain of the so-called *essential or ethereal oils*, mostly from conifer or citrus plants, *e.g.*, *oil of lemon*; various plant resins, and **india rubber** or **caoutchouc**. They are the mother substances of the individual constituents of the products just mentioned. In general usage the name *terpenes* includes not only the hydrocarbons but the various derivatives referred to above.

HYDROCARBONS

Terpenes and Hemi-terpenes.—The more common *terpene hydrocarbons* or **terpenes** in the narrow sense, such as those obtained from *oil of turpentine* and *lemon oil*, have the composition represented by the formula $C_{10}H_{16}$. This is considered as the *terpene unit* and certain members of the series which have the composition C_5H_8 are termed *hemi-terpenes*.

Olefine and Cyclic Terpenes.—Two distinct groups are known which have entirely different structure. The first and smaller group includes strictly *aliphatic hydrocarbons* belonging to the *olefine* or *ethylene unsaturated series*. The second group, which is much larger, includes *cyclo-aliphatic hydrocarbons* or as we have previously described them the *hydro-aromatic hydrocarbons*. Thus we have:

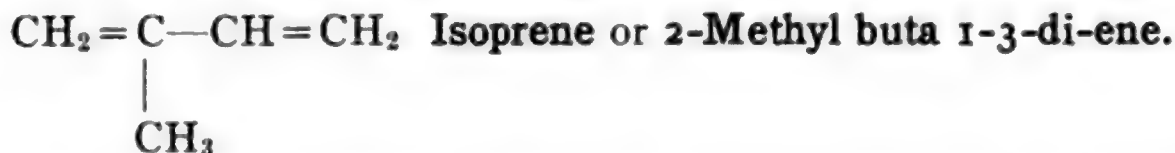
- I. **Olefine terpenes**, *open chain* compounds.
- II. **Cyclic terpenes**, *hydro-aromatic* compounds.

I. OLEFINE TERPENES

The simpler group in constitution is that of the *olefine terpenes*. This group is represented by terpenes obtained from the *ethereal oils* of *lemon*, *orange*, *rose*, *geranium*, etc., and from *india rubber* or *caoutchouc*.

Isoprene

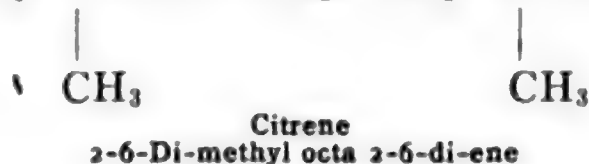
This is a terpene hydrocarbon obtained by the distillation of *caoutchouc*. It has the formula C_5H_8 and on this account is termed a *hemi-terpene*, it being one half of $C_{10}H_{16}$ the more general composition. The constitution of isoprene has been established as follows:



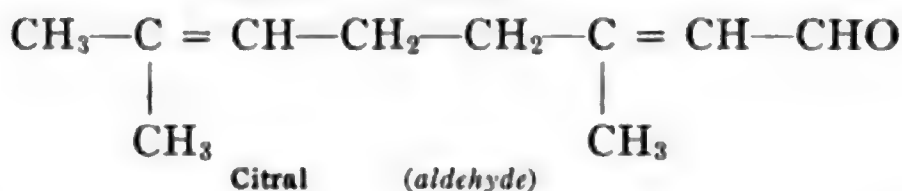
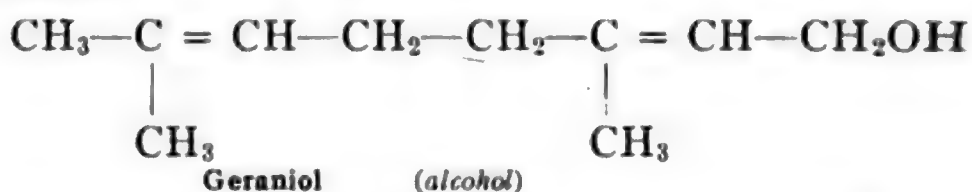
As will be discussed later this simple terpene polymerizes in forming *caoutchouc* and becomes a cyclic hydrocarbon.

Citrene and Derivatives

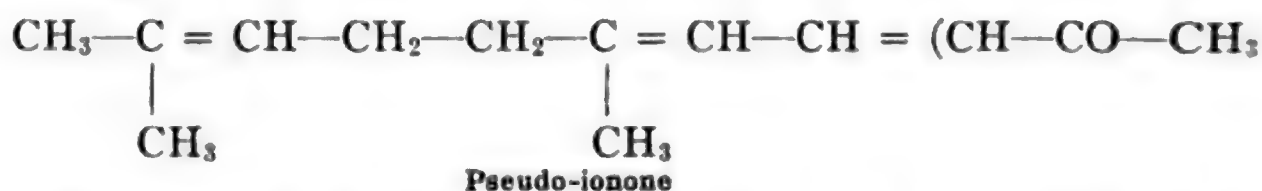
This compound is the terpene obtained from *lemon oil*. Its constitution is probably $\text{CH}_3 - \text{C} = \text{CH} - \text{CH}_2 - \text{CH}_2 - \text{C} = \text{CH} - \text{CH}_3$



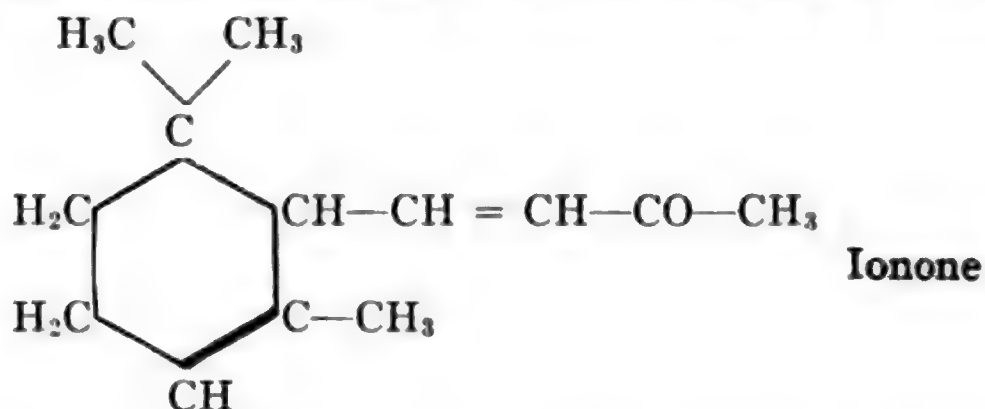
Geraniol, Citral.—Citrene by oxidation yields alcohol and aldehyde products as follows:



Geraniol is a constituent of *rose and geranium oils* and **citral** is in *lemon and orange oils* and *lemon-grass oil*. When **citral** condenses with **acetone**, with loss of water, a product known as **pseudo-ionone** is obtained.



Ionone.—This undergoes *rearrangement* with the formation of a compound with cyclic structure known as **ionone** or *artificial violet*.



These alcohol and aldehyde compounds have been previously mentioned in their proper place as unsaturated aliphatic compounds (p. 170), but are referred to again in this place because they really belong with the terpenes.

II. CYCLIC TERPENES

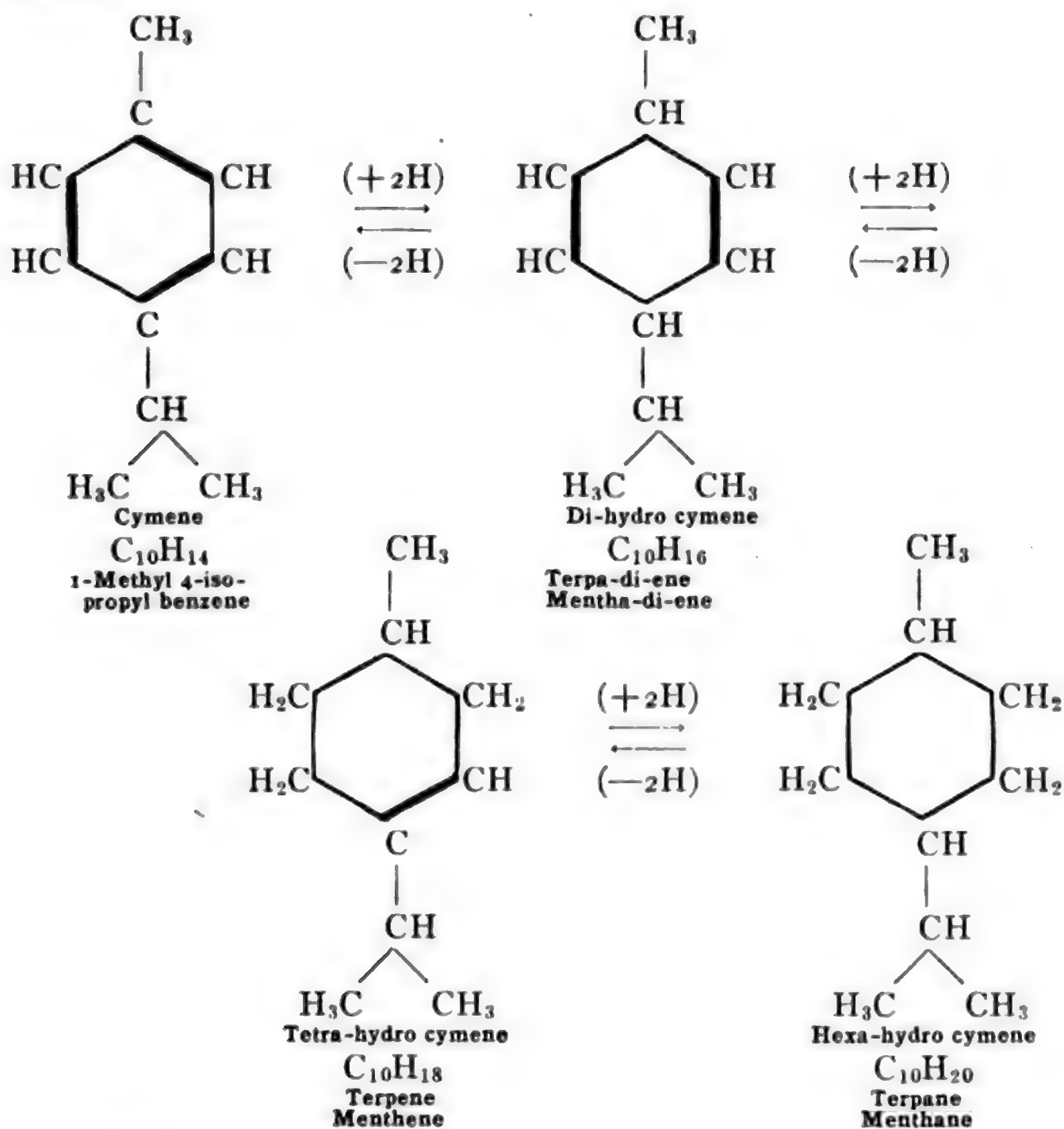
The true terpenes according to chemical constitution, and not according to properties and occurrence, are the *cyclic terpenes*. These are of two kinds, viz.:

- A. *Mono-cyclic terpenes.*
- B. *Di-cyclic terpenes.*

A. MONO-CYCLIC TERPENES

The *mono-cyclic terpenes*, as the name indicates, have the structure of a *single cycle* or *ring* of hydrogen-carbon groups.

Cymene.—When heated with iodine or with sulphuric acid some of the cyclic terpenes, *e.g.*, **pinene**, yield the benzene hydrocarbon **cymene**, **1-methyl 4-isopropyl benzene** (p. 492). All of the cyclic terpenes have been shown to be *hydrogenated derivatives* of **cymene**. These hydrogenated cymenes are of different groups depending on whether *two*, *four* or *six* hydrogen atoms have been added. These hydrocarbons and their relationship to cymene are represented by the following formulas.



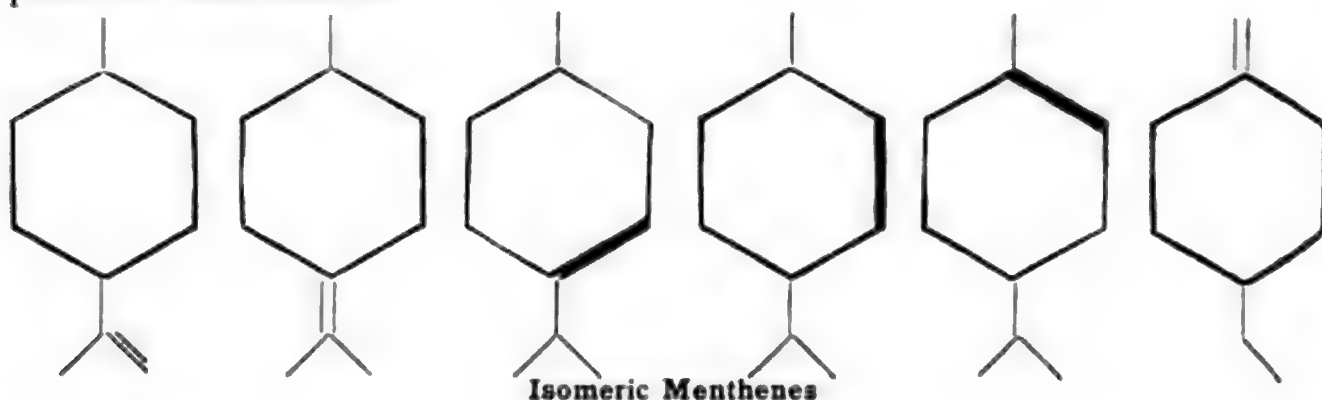
MENTHANE GROUP

The first group of mono-cyclic terpenes is known as the **menthane** group from the name of the fully hydrogenated compound *hexa-hydro cymene* which is therefore considered as the mother terpene. This compound is a *saturated* alicyclic or cyclo-paraffin compound while cymene is a benzene compound containing three double bonds. In passing from the hexa-hydro compound to the benzene compound by the loss of two hydrogen atoms at each step the compounds become more and more unsaturated as indicated by the presence of first one double bond, then two and finally three. The names given to the different compounds indicate this saturated or unsaturated condition. The saturated hexa-hydro compound is known as **menthane** or a **terpane**, the termination *ane* being the same as in the case of the saturated aliphatic hydrocarbons, the **methane** series.

MENTHENE GROUP

The *tetra-hydro cymene* containing one double bond or ethylene group is known as **menthene** or a **terpene**, while the *di-hydro cymene* containing two double bonds is named **mentha-di-ene**, a **terpa-di-ene**. The terminology and its significance will be recognized as exactly the same as used in the naming of the unsaturated aliphatic hydrocarbons (p. 161).

Isomerism.—From an examination of the above formulas it will be seen that the positions occupied by the added hydrogen atoms in the original cymene molecule or, what is the same thing, the positions occupied by the double bonds, makes isomerism possible both in the tetra-hydro cymenes or **menthenes** with one double bond and the di-hydro cymenes or **mentha-di-enes** with two double bonds. In the former case six isomers are possible while in the latter there are fourteen. This will be clear if we give the skeleton formulas for the six possible **menthenes**.



As each of these menthenes will yield isomeric mentha di-enes the number of isomers possible in this group is still larger. That is, *one menthane* yields *six menthenes* and these a larger number, viz., *fourteen, mentha-di-enes*. Furthermore, *stereo-isomerism* with accompanying *optical activity*, due to the presence of *asymmetric* carbons, increases the number of possible isomers. It will not be necessary to dwell further upon the isomerism of the terpenes it being necessary simply to explain the fact of the existence of structural isomers and of stereo-isomers with optical activity. The system of nomenclature of the isomers will not be considered. Reference to larger books will be necessary to make this plain.

In regard to menthane, the saturated hexa-hydro cymene, nothing further need be said in regard to the hydrocarbon itself. It is not a natural product but has been made synthetically by hydrogenating cymene. Its oxidation products which are natural compounds will be discussed presently. Of the menthene hydrocarbons also we need not say anything further.

MENTHA-DI-ENE GROUP

Limonenes, Terpinenes, Etc.

The most important group of the mono-cyclic terpenes is the di-hydro cymene group the members of which are known as **terpa-di-enes** or **mentha-di-enes** with the composition $C_{10}H_{16}$ which has been mentioned before as the unit terpene formula. Several of the hydrocarbons of this group are natural products in essential oils.

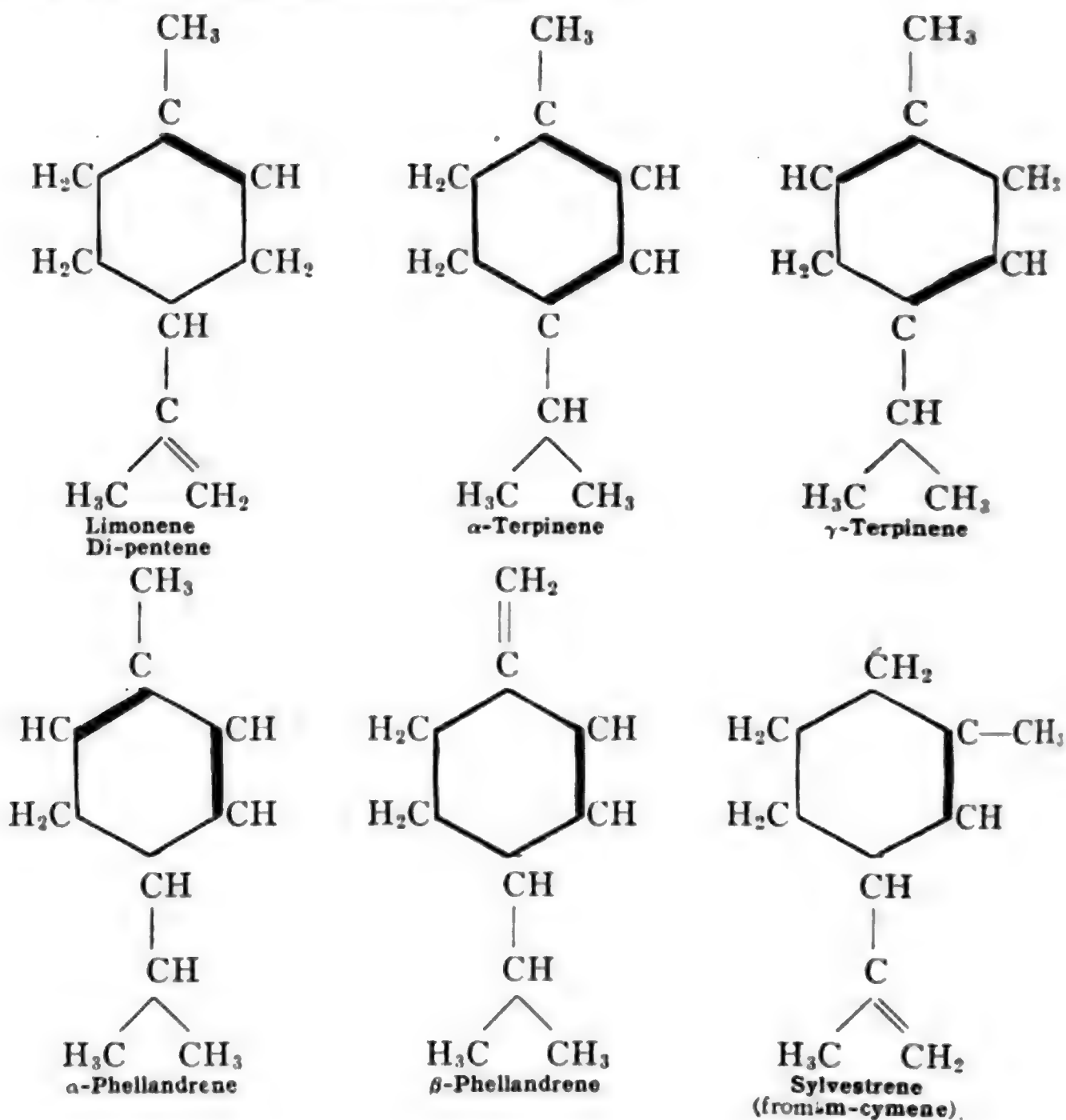
d-l-Limonene, Di-pentene.—The one occurring most commonly is **limonene**, the inactive variety of which, designated as **d-l-limonene**, is known by other names, **cinene**, **di-pentene** and **terpa-di-ene**. It is present in *Russian and Swedish turpentine*, in *pine needle oil* and in *citronella oil*. It is termed **di-pentene** because it results from the condensation of two molecules of the *pentene* known as **isoprene** or **2-methyl 1-3-buta-di-ene**. It is obtained together with isoprene when **rubber** is distilled.

d-Limonene, Citrene.—The optically active dextro variety, **d-limonene**, occurs in various essential oils and this has given to the compound different names related to the source. It is found in *lemon oil* from which it derives the name **citrene**. Its occurrence in *orange peel oil* and in *orange blossom oil*, known as *neroli oil* gives it the name **hes-**

peridene. It is found also in *cumin oil* and called **carvene**. It is present also in *bergamot, caraway* and *dill oils*.

l-Limonene.—The optically active levo variety **l-limonene** is present in *pine needle oil, American peppermint oil, American spearmint oil* and in *Russian spearmint oil*.

Terpinenes, Phellandrene, Sylvestrene.—Other less common terpa-di-enes are the **terpinenes** found in *cardamon oil*; **phellandrene** in *fennel oil* and *eucalyptus oil* and **sylvestrene** in *Swedish and Russian turpentine* and in *pine needle oil*. Sylvestrene differs from the other terpenes that have been given in that it is a derivative of **meta-cymene, 1-methyl-3-isopropyl benzene**, and not of *para-cymene*. The structural formulas of the above terpa-di-enes are as follows:

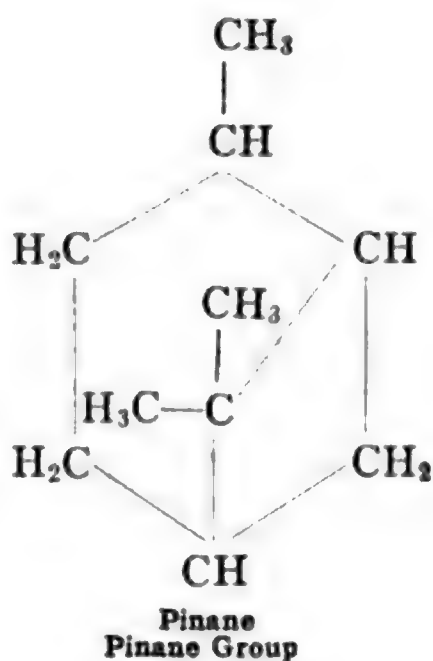
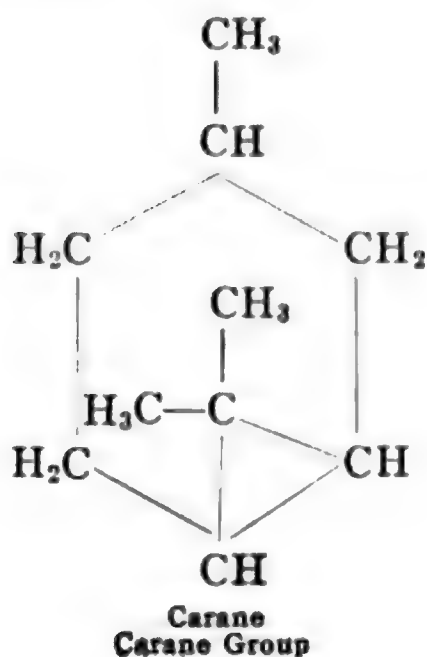


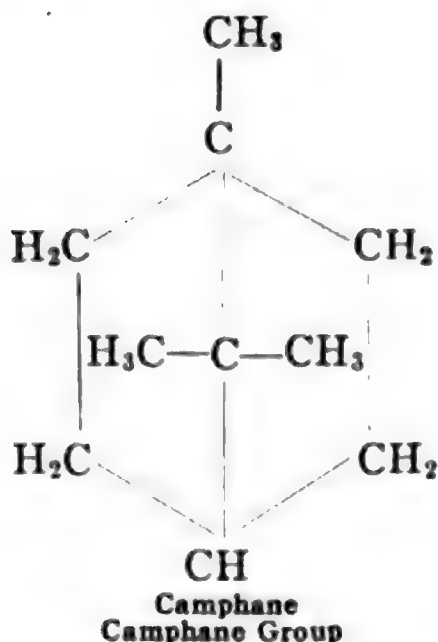
The proofs for the constitution in the case of limonene will be discussed later (p. 834).

B. DI-CYCLIC TERPENES

The *di-cyclic terpenes* are like the mono-cyclic terpenes in their derivation from **cymene** and in their general properties and occurrence. They differ, however, as their name indicates, in containing *two cyclic groups* of carbons. One cyclic group is the original benzene ring of cymene. The second results from the linkage of the isopropyl radical of cymene to a second carbon of the benzene ring.

As in the mono-cyclic terpenes so in the di-cyclic there are the three groups of compounds depending on whether two, four or six hydrogen atoms are added to the cymene. We have therefore di-cyclic terpenes derived from hexa-hydro cymene in which there is *no double bond*, those derived from tetra-hydro cymene in which *one double bond* is present and those derived from di-hydro cymene in which there are *two double bonds*. In addition to these sub-groups we have three new groups differing in the character of the second or smaller carbon cycle. Taking for illustration the hexa-hydro cymene compounds which are saturated, the names ending in *ane*, these groups and their formulas are as follows:

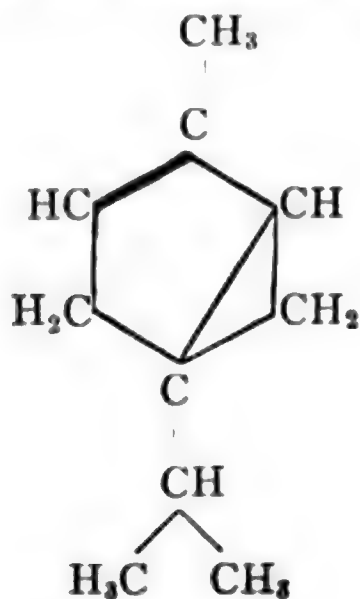




These three groups represent all of the possible structurally isomeric arrangements of such a di-cyclic compound. In **carane** there is present a *hexa-methylene ring* and a *tri-methylene ring*. In **pinane** there is a *hexa-methylene ring* and a *tetra-methylene ring*, and in **camphane** a *hexa-methylene ring* and a *penta-methylene ring*. While the saturated mono-cyclic terpenes, the *terpanes* or **menthanes**, have the composition $C_{10}H_{20}$, the saturated di-cyclic *terpenes*, above, have the composition $C_{10}H_{18}$, the two hydrogens lost being due to the second ring formed with the isopropyl group.

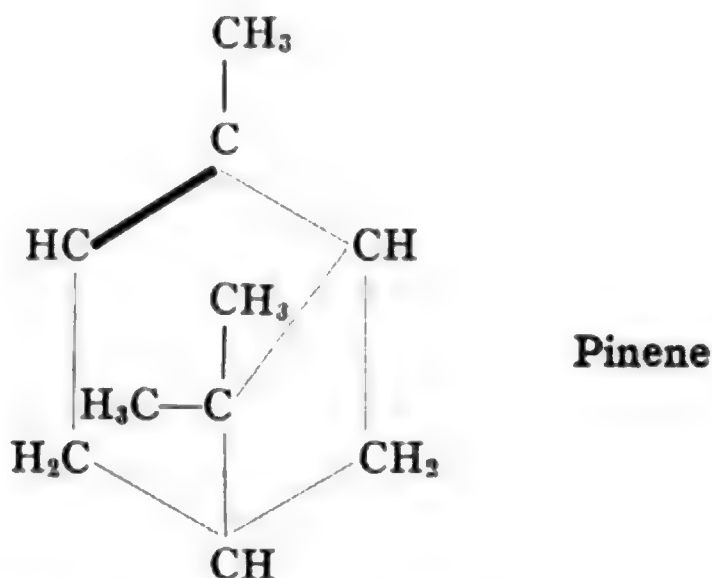
Carane, Thujene

Carane, the saturated di-cyclic terpene containing a *tri-methylene group*, is not known. An oxygen derivative is known but we need not consider it. In the unsaturated groups we find a terpene, **thujene**, with one double bond corresponding to menthene but which has a *tri-methylene group* also. This three carbon group, however, does not include the isopropyl radical but consists of three of the benzene ring carbons.



Pinane, Pinene

Similarly **pinane**, the saturated di-cyclic terpene containing a *tetra-methylene group*, is not a natural product but the corresponding unsaturated terpene with one double bond analogous to menthene is the chief constituent of *turpentine*. It is known as **pinene** and has the following constitution.



It is a characteristically smelling liquid boiling at 156° and exists in the dextro, levo and inactive forms. The dextro variety, **d-pinene**, is found in *American, Australian, Algerian and Greek turpentine* and the levo variety, **l-pinene**, in *Venetian, French and Spanish turpentine*. Being an unsaturated compound with one double linkage it unites with hydrogen chloride forming an addition product known as **pinene hydrochloride**.

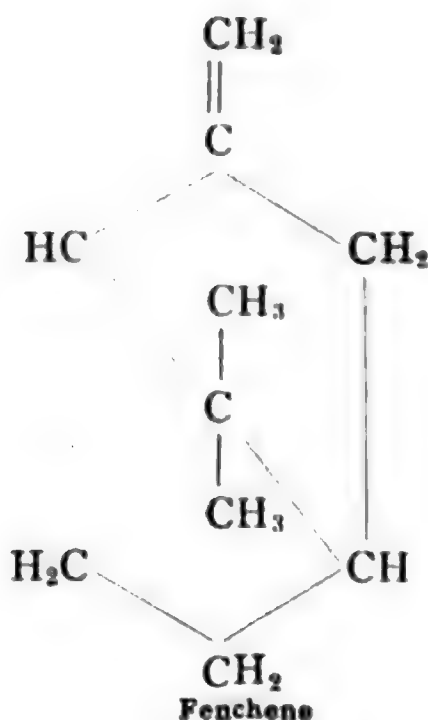
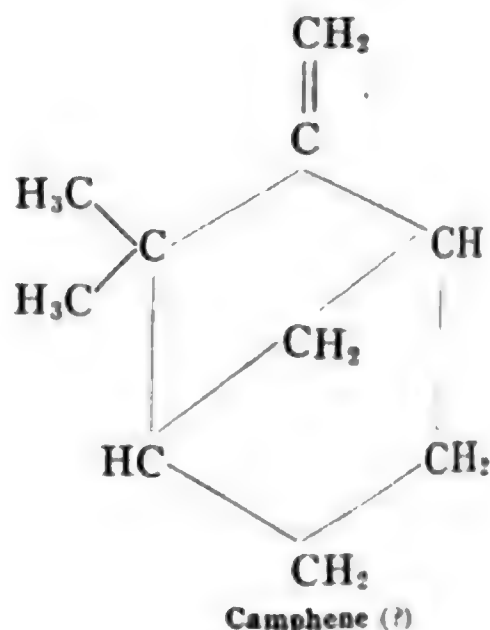
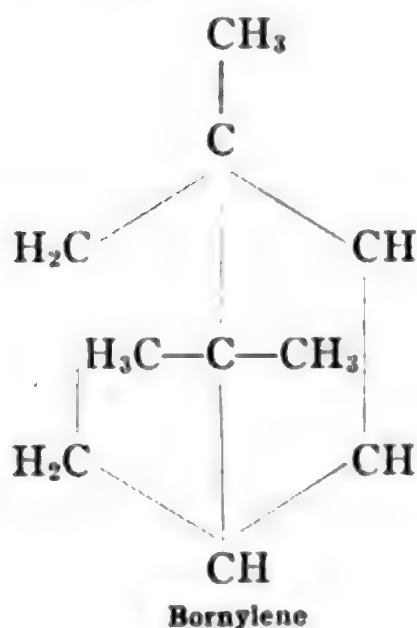
Pinene Hydrochloride. Imitation Camphor.—This substance has an odor *similar* to **camphor** and it is known as *imitation* or *artificial* camphor but it is not *synthetic* camphor. When, however, **pinene hydrochloride** is treated with alcoholic potassium hydroxide a *rearrangement* takes place followed by hydrolysis and a terpene alcohol is obtained known as **Borneol**.

Synthetic Camphor.—This by oxidation yields real **camphor**, *i.e.*, the *synthetic* compound. This synthesis will be explained in detail a little later.

Camphane, Camphene, Bornylene

The most important di-cyclic terpenes belong to the **camphane** group in which a *penta-methylene ring* is present. This five carbon

ring results from the linkage of the isopropyl radical to the *para* carbons of the benzene ring. Camphane itself is a white, volatile, crystalline compound, m.p. 154° , b.p. 160° . Three corresponding unsaturated terpenes with one double bond are known. They are **Bornylene**, **camphene** and **fenchene**. All of these have the same ring structure as camphane, the isopropyl radical linking the two *para* carbons of the benzene ring, thus forming the second ring of five carbons. Until recently the formula given below for Bornylene was assigned to camphene. Now, however, it is accepted as the true formula for Bornylene and the formula for camphene is still in doubt though the second one has been suggested.



Camphene is a solid terpene. The dextro variety **d-camphene** is found in **camphor**, *ginger* and *spike oils*, and the levo variety, **l-camphene** is in *citronella* and *valerian oil* and in *French and American turpentine*. Bornylene does not occur in nature but has been prepared from the alcohol corresponding to it known as **Borneol** or **Borneo camphor**. This, as previously stated, may be prepared from **pinene** so that Bornylene itself may be made from pinene. **Fenchene**, also, is not found in nature but is obtained by reduction of **fenchone** a terpene ketone found in *fennel oil* and in *Thuja oil*.

OXIDATION DERIVATIVES OR CAMPHORS

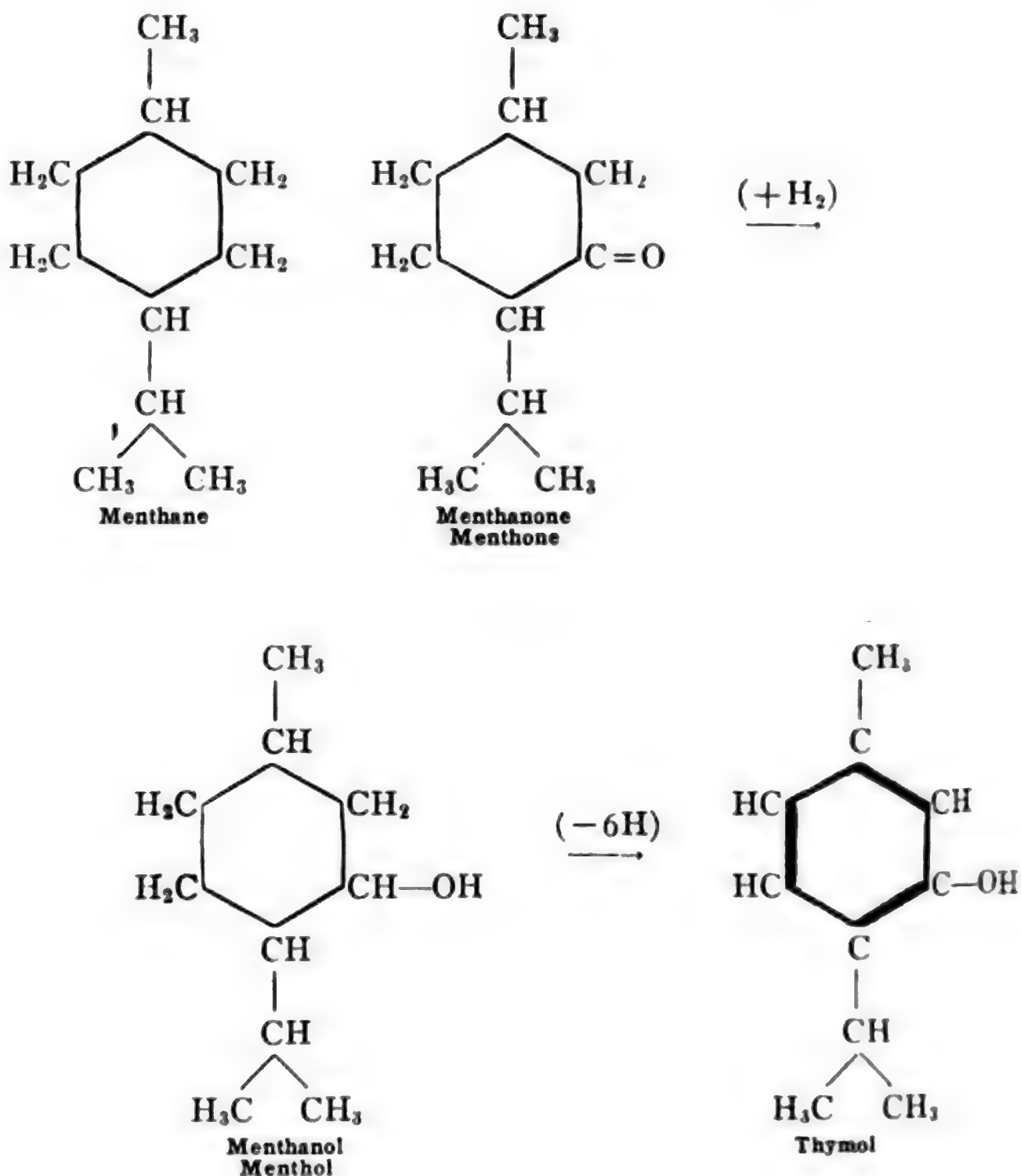
The hydrocarbons of the various groups which we have just discussed are the true terpenes. On oxidation these yield alcohol and aldehyde or ketone derivatives. The olefine terpenes, only, yield aldehydes that occur as constituents of natural products known as essential oils (p. 840). The derivatives of both groups of cyclic terpenes which are present in essential oils and plant gums and resins are either *secondary alcohols* or *ketones*. Among these latter are the *camphors* of which common **camphor** is the most important and best known example. In a general sense all of the oxidation products of the cyclic terpenes are termed camphors.

MONO-CYCLIC DERIVATIVES

Menthol, Menthone, Etc.

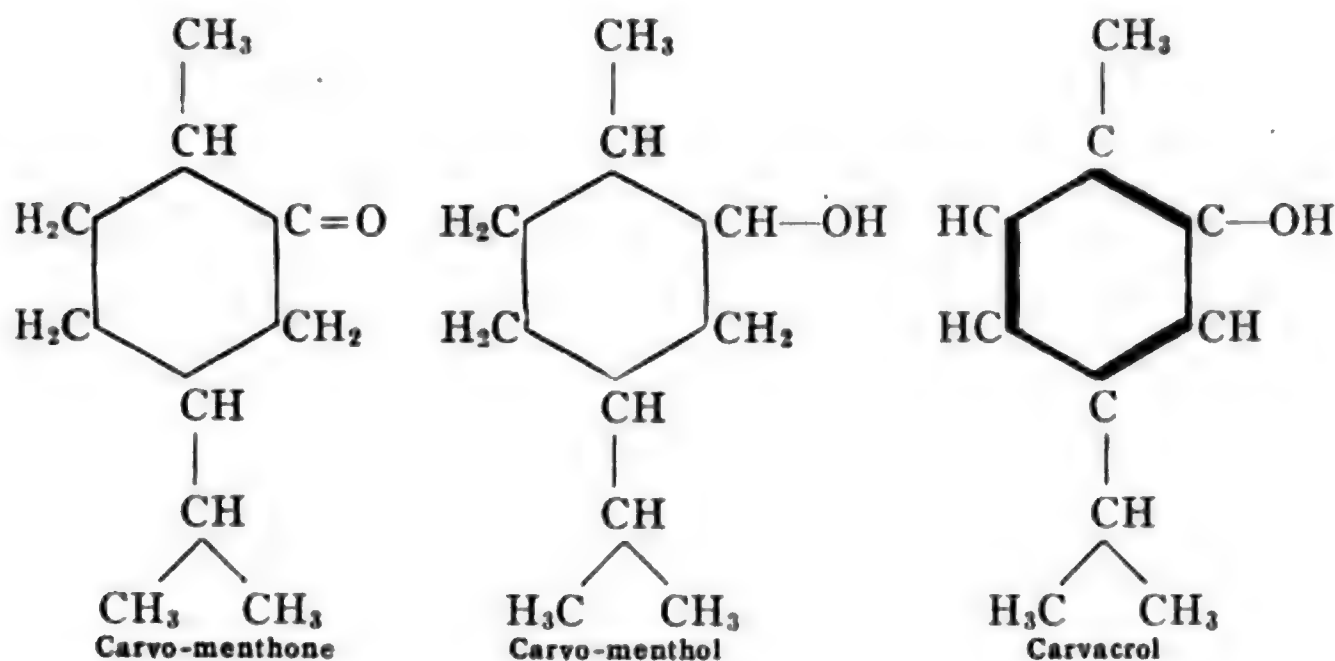
From Menthane.—Taking up these compounds in the same order in which we considered the terpenes themselves we have first the alcohols and ketones derived from **menthane**, the *saturated mono-cyclic terpene*. The more common alcohol is known as **menthol**, **menthanol** or **terpanol** and the corresponding ketone is named similarly **menthone**, **menthanone** or **terpanone**. Both of these compounds are present in *Japanese, Russian and American peppermint oil* the former occurring both as the free alcohol and as the acetic acid ester. **Menthol** is a crystalline solid, m.p. 42° , b.p. 213° . It has the characteristic peppermint odor and is used as a disinfectant and as a mild anesthetic for headache. **Menthone** is a liquid, b.p. 207° . The constitution of both compounds is proven by their relationship to **thymol**, **1-methyl 3-**

hydroxy 4-iso-propyl benzene (p. 615). **Menthone** yields **mentho** by reduction and **menthol** by loss of six hydrogen atoms is converted into **thymol**. The formulas showing these relationships are:

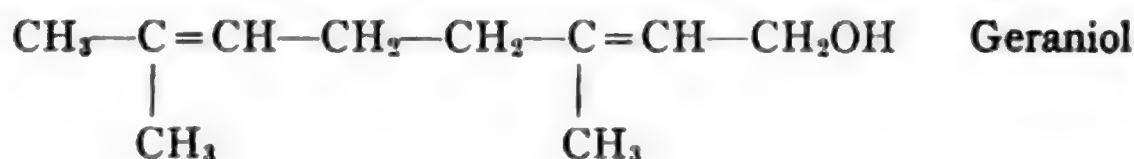


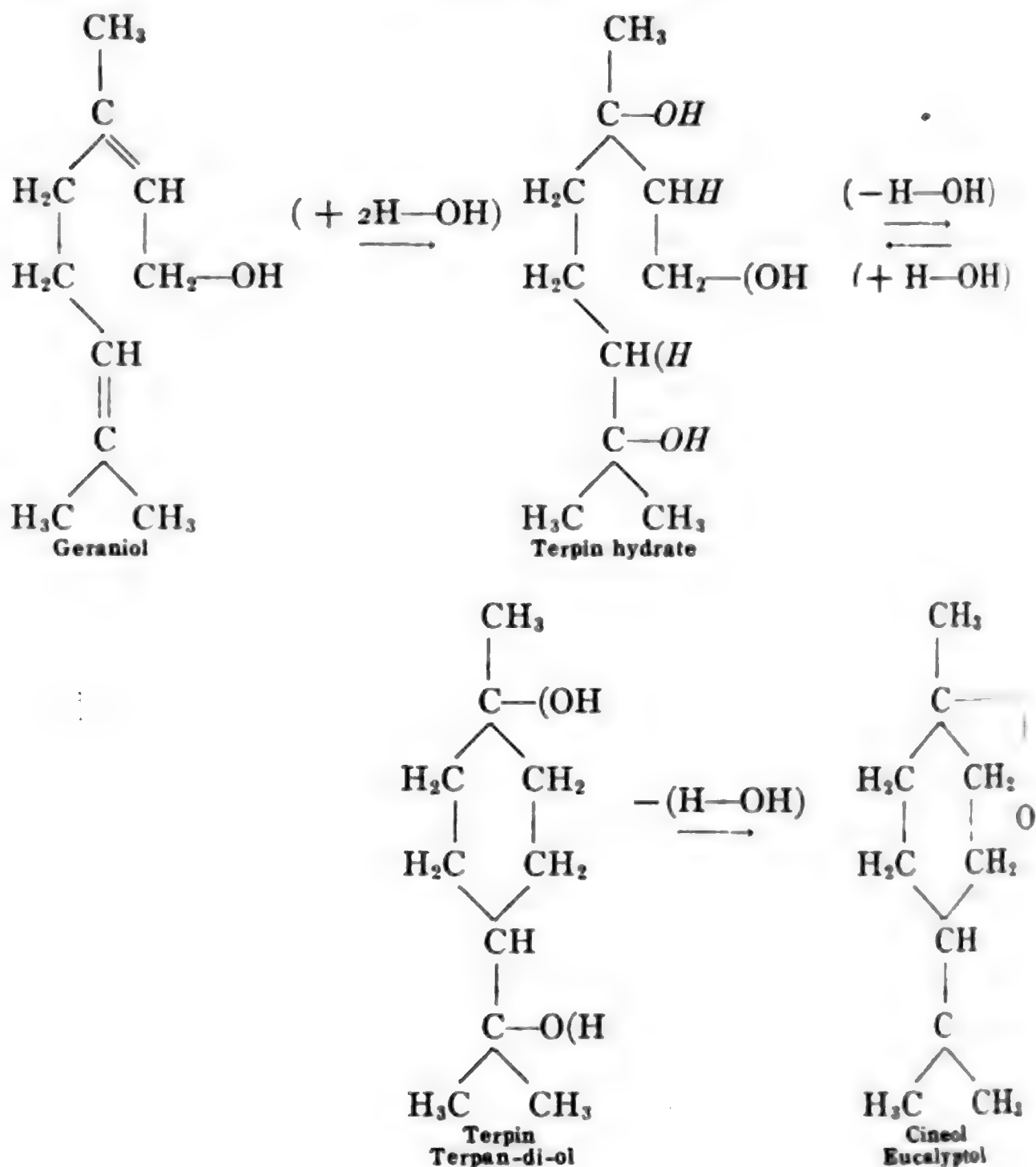
Carvo-menthol, Carvo-menthone.—Isomeric with menthol and menthone are two other compounds known as **carvo-menthol** and **carvo-menthone**. The constitution of these two is proven like the

above by their conversion into **carvacrol** (see p. 615) which is **1-methyl 2-hydroxy 4-iso-propyl benzene**. The formulas are:



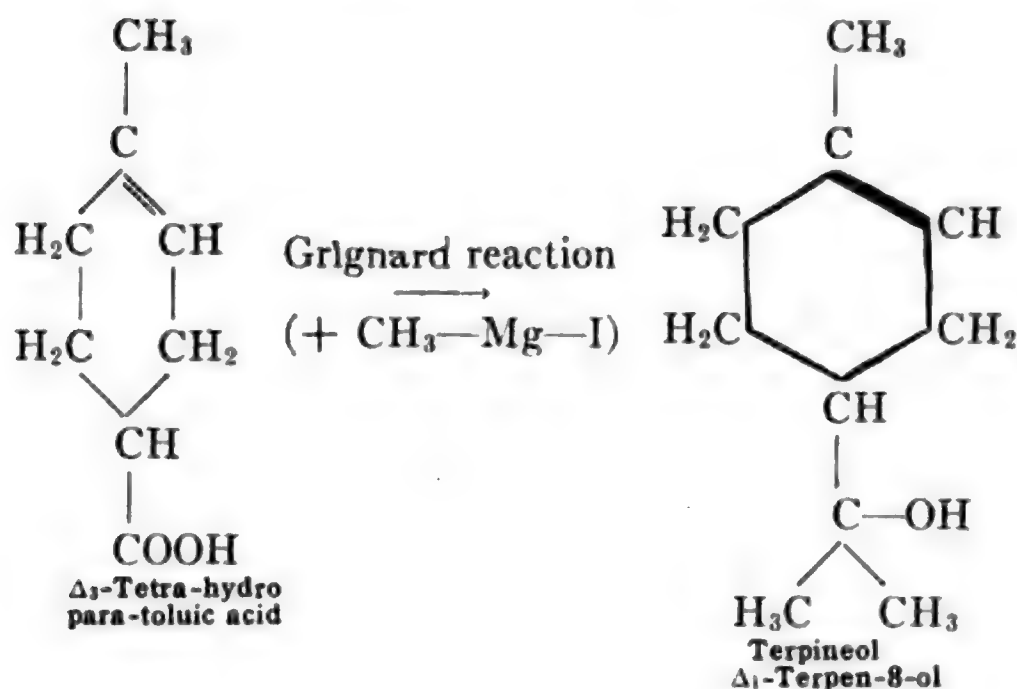
Terpin. Terpin Hydrate. Cineol.—In addition to these mono-hydroxy derivatives there is another important one which is a *di-hydroxy menthane* known as **terpan-di-ol** or **terpin**. Terpin boils at 258° and readily forms a crystalline hydrate, **terpin hydrate**, which melts at 117° . It also loses water yielding an anhydride known as **cineol**. Terpin and terpin hydrate are obtained from the terpenes in *oil of turpentine* by the action of acids. Cineol is found in *eucalyptus oil*. The constitution of these compounds is proven by their relation to **geraniol** (p. 167). When treated with 5 per cent H_2SO_4 two molecules of water are added to **geraniol** and **terpin hydrate** is formed. This by loss of one molecule of water forms a closed ring yielding **terpin** and this by loss of another molecule of water yields **cineol**. These relationships are as follows:



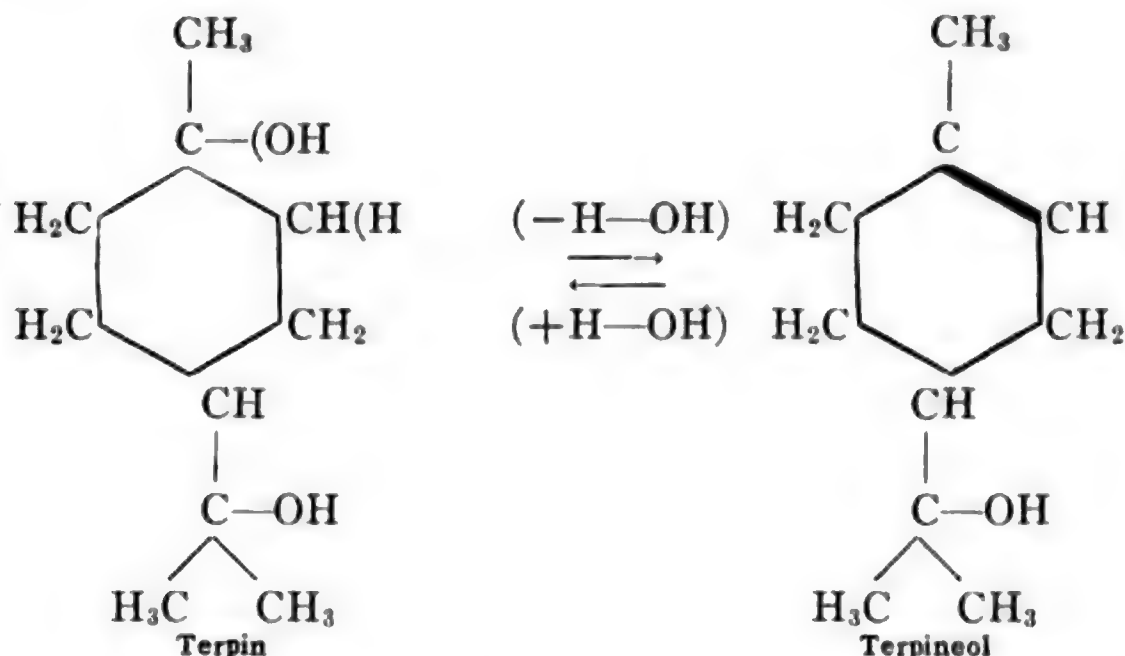


Terpineol, Etc.

Derivatives of Menthene.—The most important alcohols and ketones derived from the **menthene** unsaturated group of terpenes are **terpineol**, **di-hydro carveol**, **di-hydro carvone** and **pulegone**. The first one, the alcohol **terpineol**, occurs in its *dextro* form in *cardamon oil* and *marjoram oil*, in its *levo* form in *neroli oil* and in its *inactive* form in *cajeput oil*. The constitution is proven by **Perkin's** synthesis from Δ_3 -tetra-hydro para-toluic acid by means of the Grignard reaction.

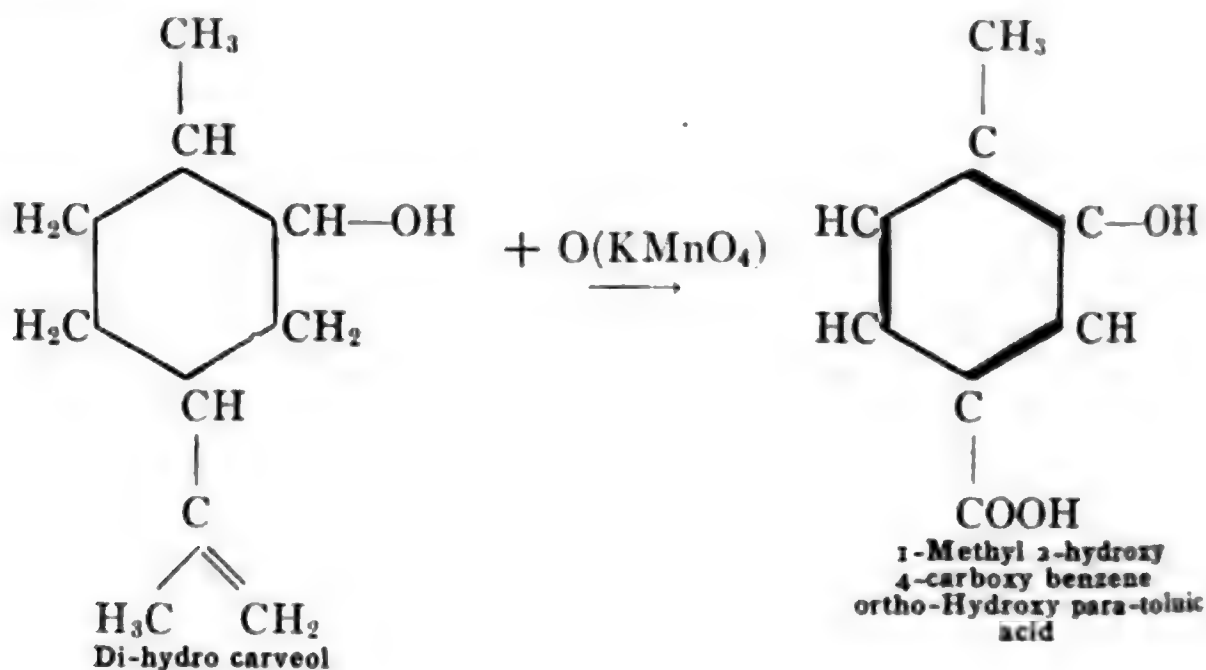


This constitution is supported also by the conversion of terpineol into terpin and vice versa. When **terpin** loses a molecule of water, not from the two hydroxyl groups, as in the preceding conversion into cineol, but in such a way as to leave one hydroxyl group present, we obtain **terpineol**.



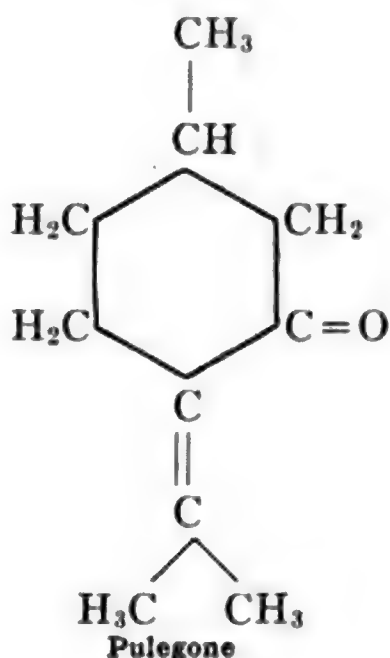
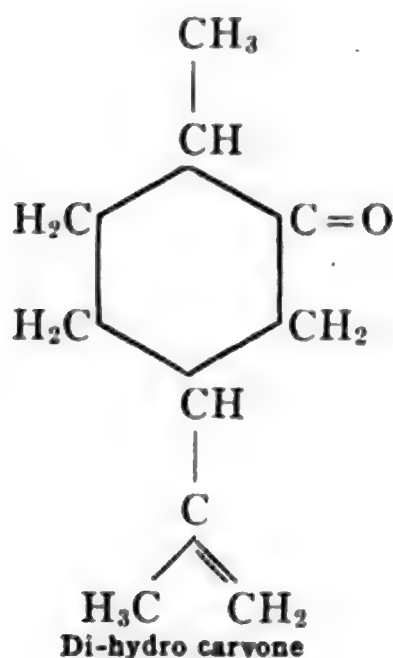
Di-hydro Carveol, Di-hydro Carvone.—**Di-hydro carveol**, the other important **menthen-ol**, is present in *kummel oil*, together with the corresponding ketone, **di-hydro carvone**, from which it may be obtained by reduction. This ketone is the di-hydrogen addition product of a **mentha-di-ene** ketone known as **carvone** which we shall presently consider.

Position of the Double Bond.—Two points must be established in connection with the constitution of these menthene compounds, viz., the *position of the hydroxyl and ketone groups* and the *position of the double bond*. Both of these points are proven by the following oxidation of **di-hydro carveol** to **1-methyl 2-hydroxy 4-carboxy benzene**.



This oxidation is accomplished by means of potassium permanganate, a reaction which is characteristic of compounds containing a doubly bound group resulting in the splitting of the compound at the double bond. The first product formed results from the addition of two hydroxyl groups, one to each carbon originally doubly linked. Further oxidation then splits the compound and converts the remaining carbon group into carboxyl. After the removal of the added hydrogen of the menthene compound the resulting **ortho-hydroxy para-toluic acid** is obtained. The *position of the ethylene group* in **di-hydro carveol** must therefore be *in the iso-propyl radical* as the tertiary carbon of this radical remains as carboxyl in the resulting toluic acid. Also the *hydroxyl group* in the di-hydro carveol must be in the *ortho* position to the *methyl group* and *meta* to the *iso-propyl group*. The entire constitution is thus established and as **di-hydro carvone** is the ketone corresponding to di-hydro carveol the constitution of the former is likewise proven. The position of the hydroxyl and ketone groups in these two compounds is also proven by the fact that they each yield **carvacrol** or hydroxy cymene in which the hydroxyl group is *ortho* to

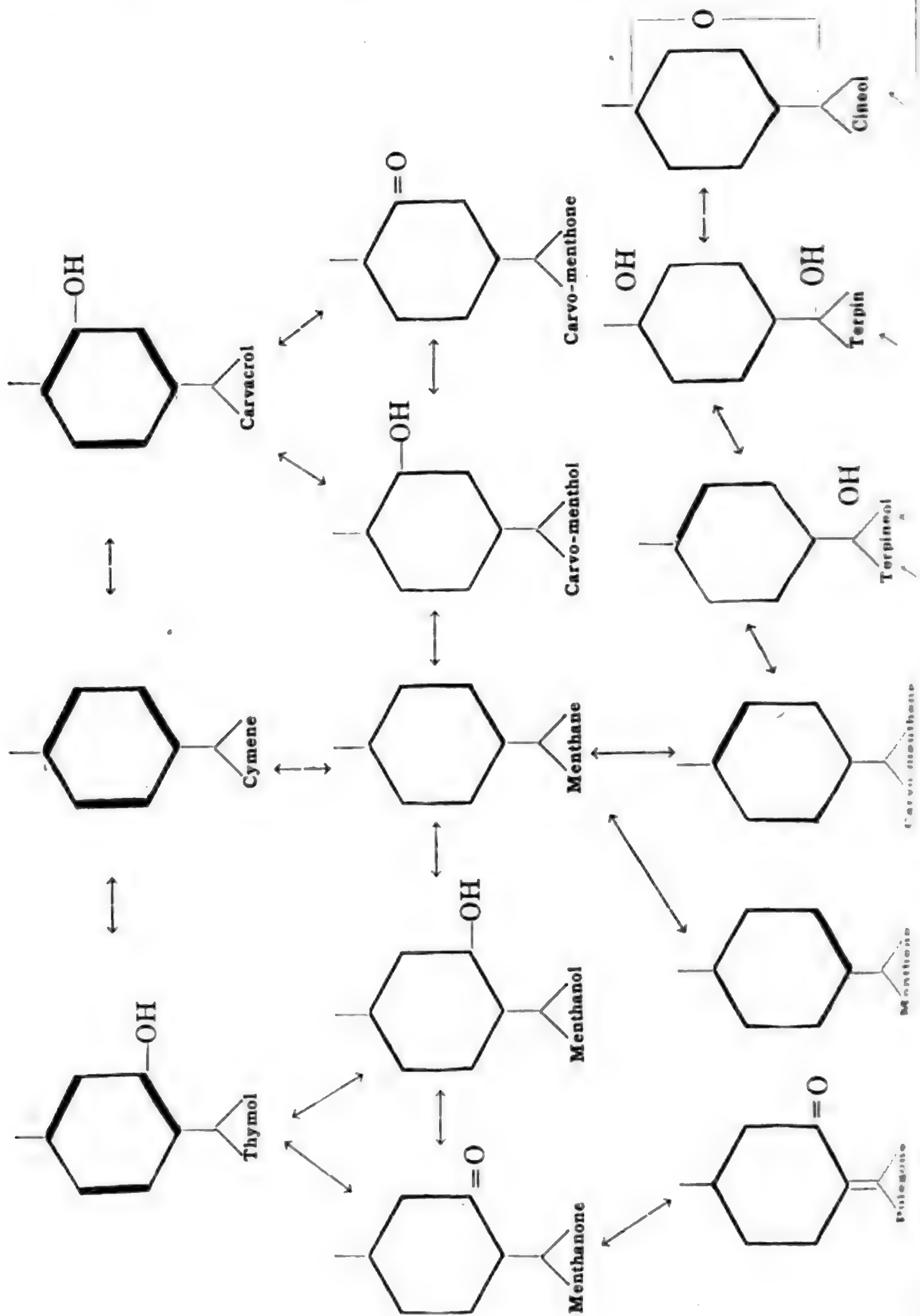
methyl and *meta* to iso-propyl. The formula of di-hydro carvone is given below together with that of the other menthene ketone known as pulegone.

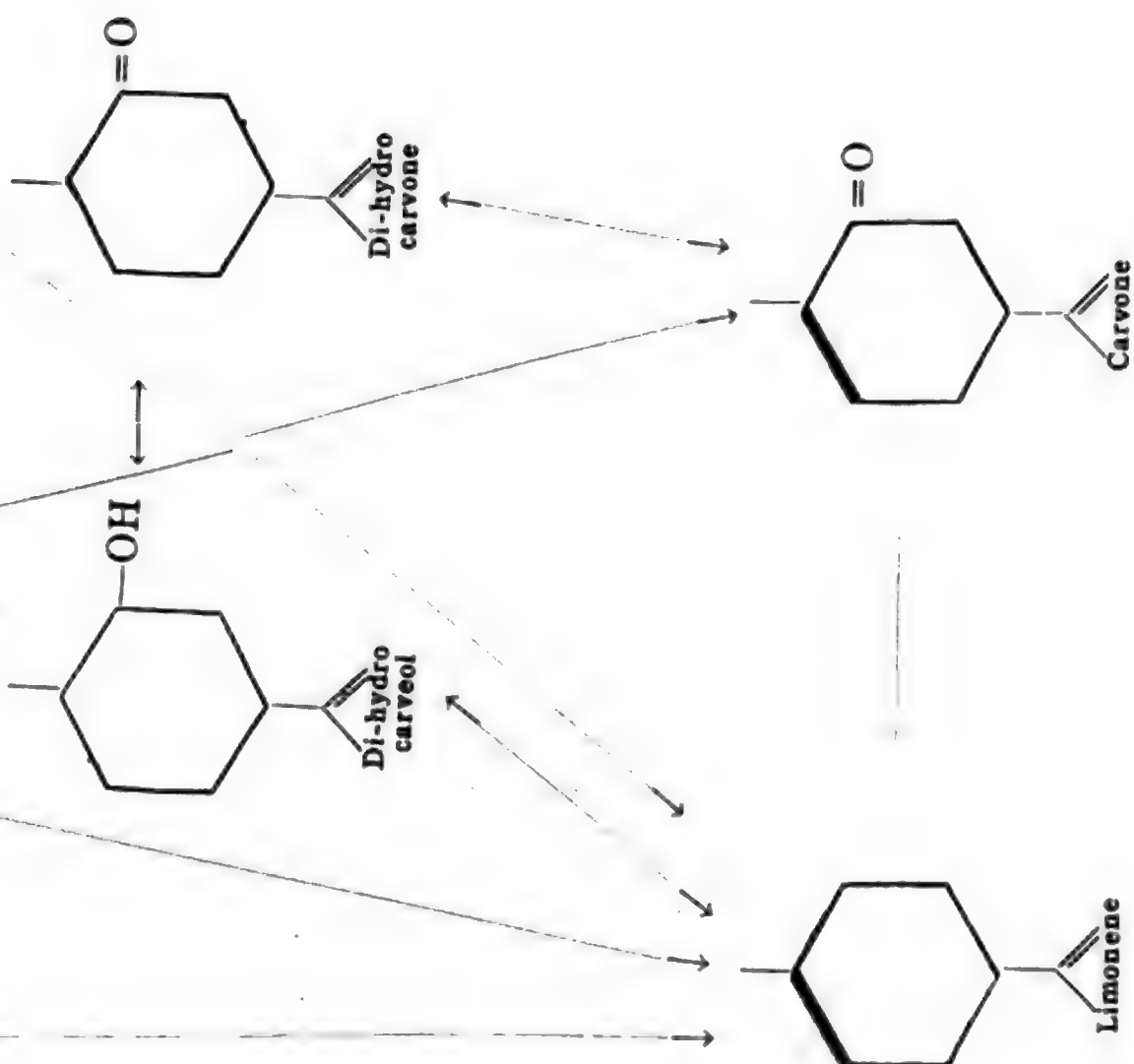


Pulegone.—Pulegone is present in *pennyroyal*, *Mentha pulegium*. It yields **menthone** by addition of two hydrogens, which, by reduction, yields **menthol**, and this, by loss of hydrogen, is converted into **thymol**. The position of the ketone group is thus proven.

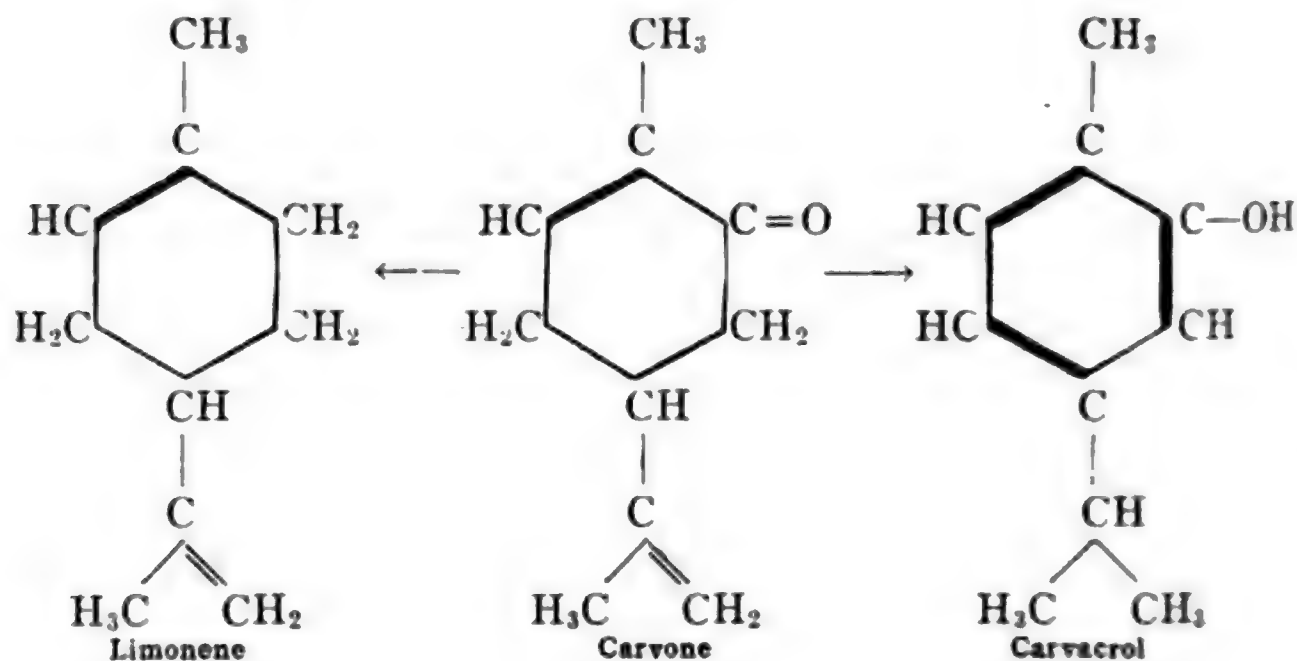
Carvone

Mentha-di-ene Ketones.—Among the terpene hydrocarbons the most numerous and most important members belonged to the **mentha-di-ene** group characterized, it will be recalled, by the presence of *two double bonds*. Among the oxidation products, however, there is only one belonging to this group which we shall mention. This is a ketone known as **carvone** which is present in *kummel oil* and in *dill oil*. The relationships of this ketone are very important and help to establish the constitution of the mentha-di-ene hydrocarbons, **limonene**, **terpineol**, etc. (p. 820). The constitution of carvone itself is proven by its relationship to the menthene alcohols and ketones. As the names indicate, **carvone** is related to **di-hydro carvone**, which it yields on the addition of two hydrogen atoms, and to **di-hydro carveol** the corresponding alcohol. Also carvone may be converted into **terpineol** which is isomeric with di-hydro carveol. The constitution of these two





menthene alcohols is proven as recently shown (pp. 829, 830) by their relationship to derivatives of **para-toluic acid**. In them the position of the one double bond is different, so that as carvone yields either of them, its two double bonds must be in the two positions, one as in di-hydro carveol and the other as in terpineol. Furthermore, the position of the ketone group in carvone must be the same as in di-hydro carvone and the same as the hydroxyl group in di-hydro carveol. This is also proven by the fact that carvone, by heating with potassium hydroxide or phosphoric acid, yields a benzene phenol, isomeric with **thymol**, viz., **carvacrol**, 1-methyl 2-hydroxy 4-isopropyl benzene. Thus the formula for **carvone** is as given below with its relation to carvacrol and and to limonene.



As **carvone** may be converted into **limonene**, a mentha-di-ene hydrocarbon, the constitution of the two must agree and the formula for the latter is as above which is the same as previously given to it (p. 820). Limonene is thus the mother terpene of carvone.

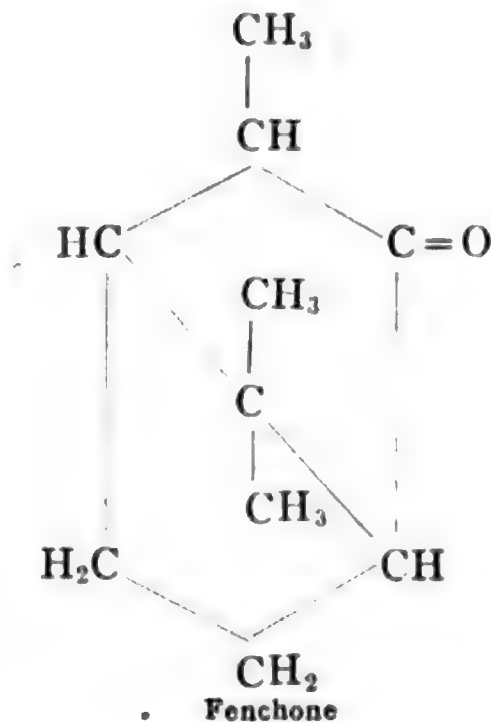
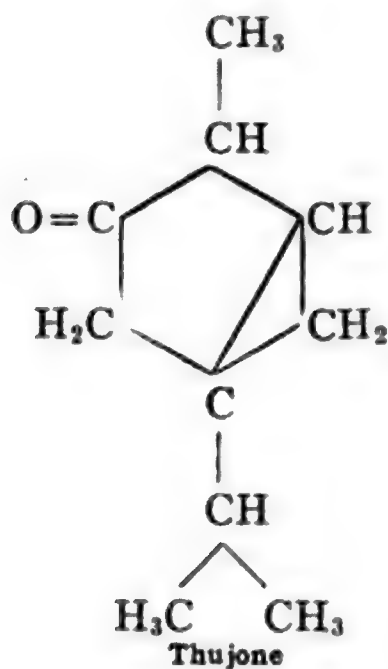
The preceding tabular scheme of the mono-cyclic terpenes and their oxidation products shows the relationships which we have been discussing.

DI-CYCLIC DERIVATIVES

Borneol, Camphor

The most important of all of the oxygen derivatives of the terpene hydrocarbons are those of the di-cyclic group. Of these the most common is the well-known substance **camphor**, also termed **Japan camphor**. It is a ketone derivative of a di-cyclic terpene of the camphane type known as **Bornylene**. The corresponding alcohol derivative is known as **Borneol**, or *Borneo camphor*.

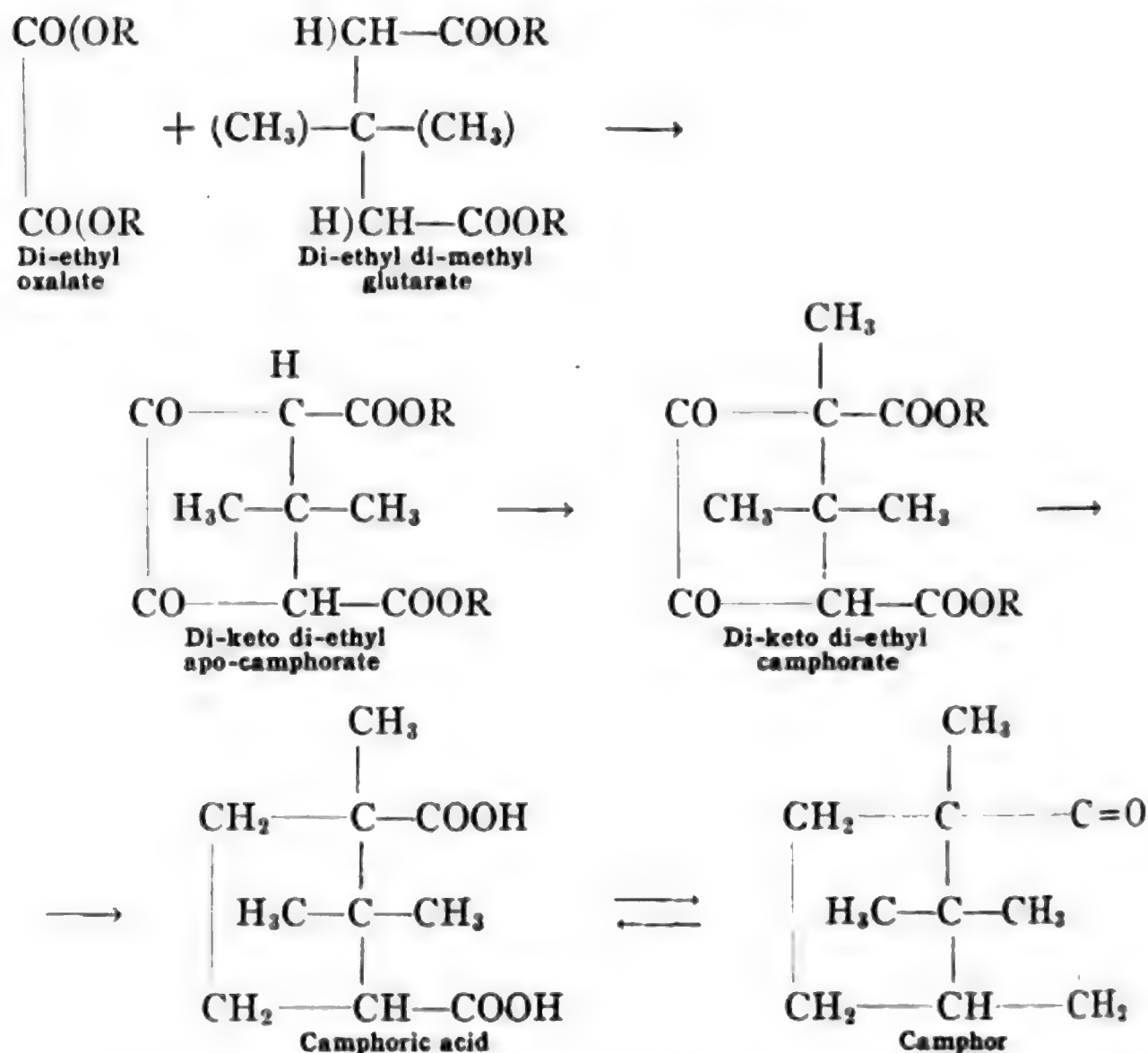
Thujone, Fenchone.—Two other ketone derivatives are known, viz., **thujone** and **fenchone**. They occur together in *thuja oil*. Thujone is present also in *tansy*, *wormwood* and *sage oils* while fenchone is found in *fennel oil*. Without taking up the proofs for the constitution of these two ketones we may give their formulas as below:



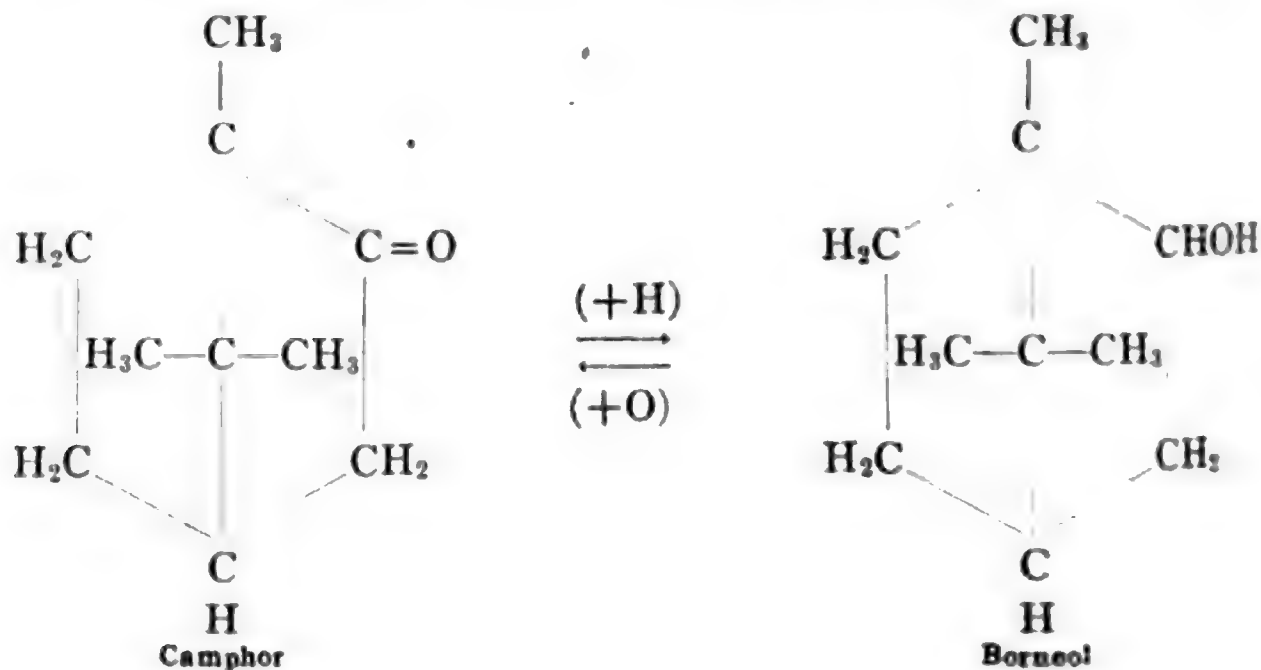
They are derivatives of saturated di-cyclic terpenes which in turn are related to the unsaturated di-cyclic terpenes **thujene** and **fenchene** which we have previously discussed (p.p. 822, 824).

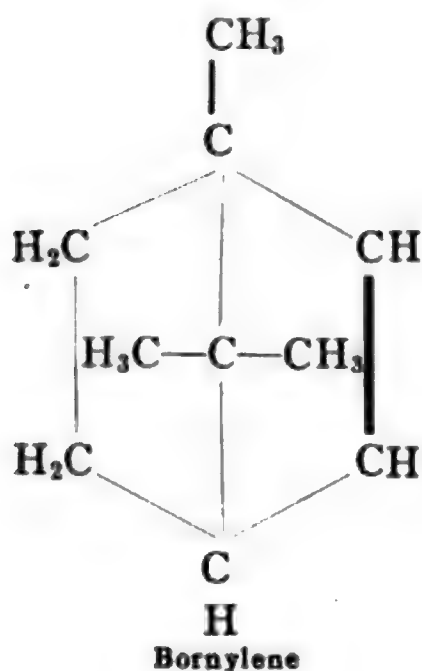
Constitution of Camphor.—The constitution of **camphor** and of **Borneol** has been established by **Kompa's synthesis** of **camphoric acid** which is obtained by the oxidation of camphor.

Kompa's Synthesis of Camphoric Acid.—The synthesis of camphoric acid is accomplished by starting with **di-ethyl oxalate** and condensing it with the di-ethyl ester of **di-methyl glutaric acid**.



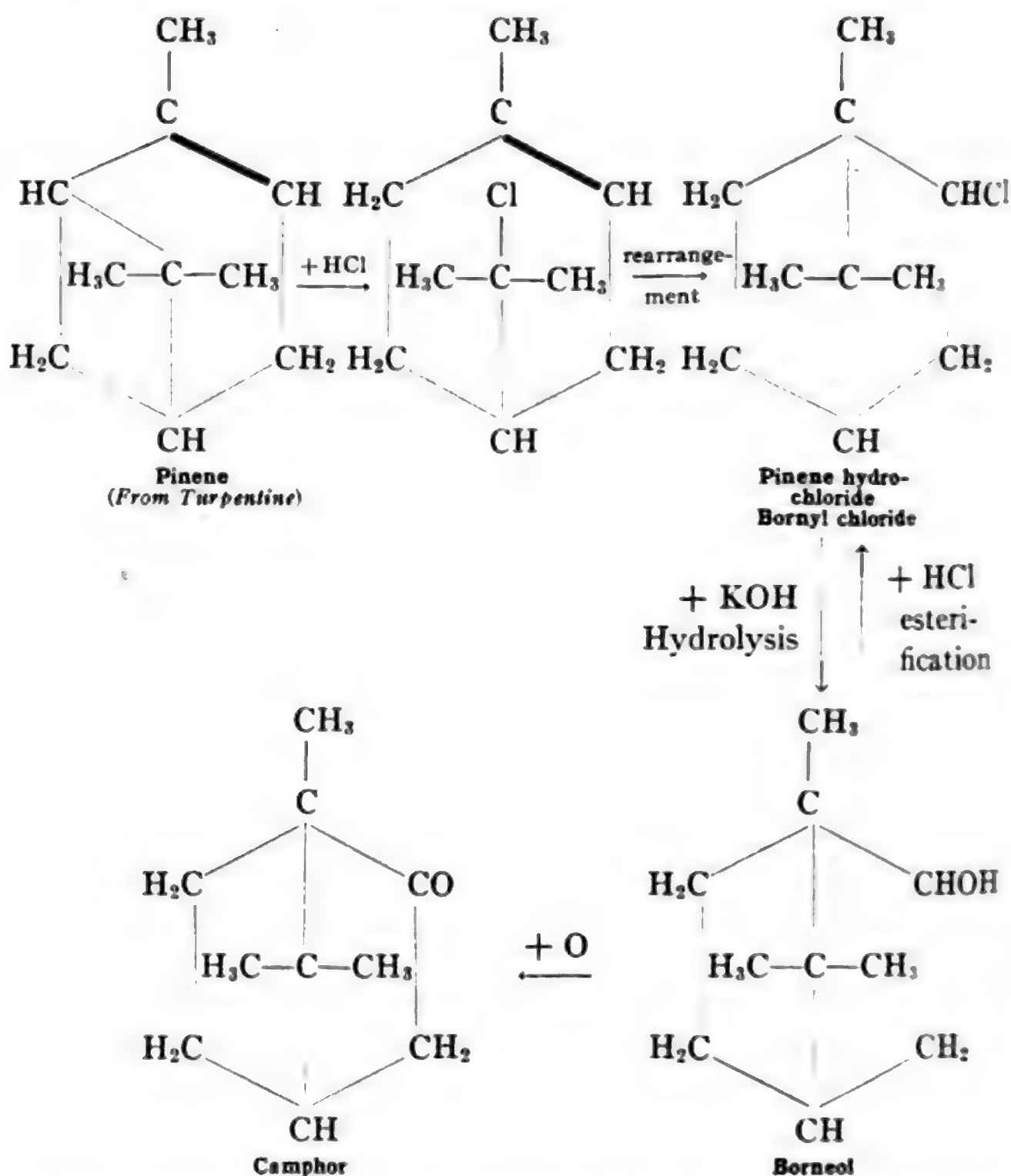
Thus camphor, writing the formula as a terpene, has the following formula and Borneol that of the corresponding alcohol.





Camphor and **Borneol** are therefore derived from a **camphane** di-cyclic terpene in which the isopropyl group joins the *para* carbons. The unsaturated di-cyclic terpene corresponding to camphor was at first supposed to be camphene but later work has proven that it is not camphene but **Bornylene** which has the structure corresponding to camphor. The constitution of camphene is still unestablished.

Synthesis of Camphor.—The relationship of **camphor** to **pinene**, the terpene present in turpentine, is of especial interest and importance in connection with its synthesis. Pinene is the unsaturated di-cyclic terpene related to the saturated di-cyclic terpene **pinane** (p. 823). In both of these terpenes the di-cyclic arrangement is different from that in **camphane** and **Bornylene** in that the isopropyl group in forming the secondary cycle joins the *meta* carbons instead of the *para*. Now pinene, by addition of hydrogen chloride, forms a hydrochloride which has been referred to as artificial camphor. This hydrochloride is identical with the hydrochloric acid ester of Borneol and may be converted into Borneol by hydrolysis. Now as Borneol can be oxidized to camphor we may thus obtain true synthetic camphor from pinene. The reactions, involving an intermediate product and then rearrangement of the secondary cycle in pinene, are as follows:



These reactions, in principle, are those used in the commercial synthesis of camphor and show the relationship of the intermediate products. The details of the methods actually used are various and may be found by consulting larger books. The pinene is obtained from turpentine, the turpentine itself being used directly. The production of synthetic camphor from this source has been developed very much during recent years.

Natural Camphor.—Camphor is obtained as a natural product from the camphor tree, *Laurus camphora* (or *Cinnamomum camphora*).

which grows chiefly in Japan, China and Formosa. It is obtained from trees 30-40 years old, being present in the wood somewhat similarly to turpentine in pines. Being a solid instead of a liquid it must be extracted from the wood with boiling water, or by distillation with steam. On cooling the hot water extract or distillate the camphor separates as a white crystalline mass. This crude product is refined by heating it with charcoal and lime when pure camphor sublimes. It is a white, bitter, rather soft crystalline substance, melting at 178° and boiling at 207° , but subliming slowly at ordinary temperatures. Borneol or Borneo camphor is the corresponding alcohol. It is very similar to camphor in its properties.

In 1907 about 4,300,000 kilos of camphor were produced in Japan and Formosa where the industry is a state monopoly. New plantations of trees are planted each year, some 5,000,000 being set out in 1909.

The world's consumption of camphor is about 5000-6000 tons. Camphor is also produced somewhat in Italy and in Florida and Texas. Most of the camphor is utilized in the manufacture of celluloid (p. 376), about 70 per cent of the product being thus used under normal conditions. About 2 per cent is used in the manufacture of explosives, to make them insensitive to shock; 13 per cent for pharmaceutical preparations and 15 per cent for miscellaneous purposes. Its most common use is as an insecticide for the moth larvæ in which use it is largely replaced by naphthalene in the form of moth balls.

Turpentine Industry

It has been previously stated that the terpenes as natural products are found in the essential oils of various plants especially conifers and citrus plants. The most common and abundant natural product of this nature is **turpentine** which is the essential oil of various conifer trees, certain *pin*es, *firs* and *larch*es. Turpentine is also termed American, French, Venetian, etc., according to the locality of growth. The turpentine is obtained from the tree by cutting incisions and collecting the juice. In some cases the wood is cut up and distilled directly. Crude turpentine becomes resinous on standing. On distilling the crude product with steam pure turpentine or *oil of turpentine* (essence of turpentine) passes over leaving behind a solid resin known as *rosin* or *colophony*. Pine oil of turpentine is a clear, colorless liquid of

characteristic odor. It boils at 156° but readily volatilizes in the air especially when spread in a thin layer. On standing in the air it resinifies somewhat. It is a good solvent of resins, rubber, phosphorus and sulphur. Its principal use is in varnishes and paints. In both varnishes and paints the turpentine is used as a thinning agent. Varnishes consist of various resins (*copal*, *rosin*, *shellac*) dissolved in oil, which acts as dryer, and this mixture is thinned with turpentine. In paints various pigments are similarly dissolved in drying oils and thinned with turpentine. When spread in a thin layer the turpentine readily evaporates leaving the resin of the varnish and the pigment of the paint spread in a thin layer mixed with the drying oil which on oxidizing forms a hard smooth surface coating. Rosin or colophony varnishes are poor in quality compared with those made from *copal resin*. *Shellac* or *lac*, a resin obtained from certain Indian trees, is used chiefly dissolved in methyl alcohol as a *spirit varnish*. The principal terpene in turpentine is **pinene**. As this is optically active, the turpentine itself is dextro or levo according to which pinene predominates. United States, France, England, Germany and Russia are the principal countries producing it. In 1909 there were 1585 turpentine distilleries in the United States producing about 580,000 barrels valued at about \$25,000,000 and in 1911 the United States exported about 18,000,000 gallons. One cubic meter of fir yields 10 kilos of crude turpentine which in turn yields 7 kilos of rosin and 3 kilos of oil of turpentine. One cubic meter of pine yields 22 kilos of crude turpentine yielding 16 kilos rosin and 6 kilos of oil of turpentine. Larch yields between these two.

Rosin—Colophony.—The solid resin left as a residue when crude turpentine is distilled is known as **rosin** or **colophony**. It is a hard, brittle resin, too brittle to make a good varnish. The chief uses of rosin are in soap making (resin soaps), varnishes, sealing wax and in sizing paper. Sealing wax is a mixture of rosin, shellac, turpentine and mineral substances such as chalk, burnt gypsum, kaolin, etc.

ESSENTIAL OILS AND PERFUMES

In the preceding discussion of the terpenes we have frequently referred to *essential oils* or as they are also termed *ethereal oils*. These names, however, do not apply to a distinct chemical group of com-

pounds but to a group of products which are obtained from plants by similar processes of extraction and which possess certain general characters in common. They are usually more or less volatile, aromatic substances possessing an odor which is often distinctive of the plant from which they are obtained. Being both volatile and aromatic they are used in the manufacture of perfumes. The compounds isolated from these essential oils are therefore the odoriferous constituents of the flowers and other parts of certain plants. These compounds belong to various classes, viz.: *esters*, *aldehydes*, *ethers* and *terpenes*, the latter including both the hydrocarbons and their oxidation products. Therefore, while the consideration of the essential oils is not connected solely with the discussion of the terpenes, yet it has been best to postpone any general treatment of the subject until the terpenes had been considered.

Esters.—The simplest class of compounds present in essential oils are the *esters* or *ethereal salts* (p. 140). In our early discussion of these compounds in the aliphatic series it was stated that the odor and flavor of common fruits is probably due to ester compounds and that certain empirical mixtures of esters are used as artificial fruit essences. Artificial apple essence, for example, may be prepared by mixing certain proportions of **ethyl nitrite**, **ethyl acetate** and **amyl valerate** with chloroform, aldehyde and alcohol. An example of an essential oil which consists of a single ester is *oil of wintergreen* which is the *methyl ester* of **salicylic acid**, **ortho-hydroxy benzoic acid** (p. 714).

Aldehydes.—Some essential oils contain *aldehydes*, e.g., *oil of bitter almonds*, which is **benzaldehyde** (p. 654). *Oil of cinnamon* and *oil of cassia* contain mostly **cinnamic aldehyde** (p. 656).

Ethers.—*Ethers* are also constituents of essential oils either as simple ethers or as mixed ether-alcohol or ether-aldehyde compounds. Examples of such oils are *oil of anise* containing **anis aldehyde** and **anethole** (p. 661), and *oil of clove* which contains **eugenole** (p. 623).

Olefine Terpenes.—The *olefine terpenes* and the alcohols and aldehydes derived from them are found in several essential oils, e.g., *oil of geranium* contains **geraniol** and **citronellol** (p. 167), and *oil of lemon*, **citral** and **citronellal** (p. 170).

Cyclic Terpenes.—The *cyclic terpenes* and their oxidation derivatives such as **pinene**, **limonene**, **menthol**, **terpineol**, **cineol**, **carvone**, **fenchone** and **camphor** are found in a large number of essential oils

such as *turpentine*, *oil of peppermint*, *oil of lemon*, *oil of caraway*, *fennel oil*, *camphor*, etc.

The following table gives some of the more common essential oils with their source and their chief constituents.

TABLE XX.—ESSENTIAL OILS

Oil	Source	Chief constituents
<i>Fruit essences</i>	Common fruits.....	Mixtures of simple esters of mono-basic acids and mono-hydric alcohols.
<i>Oil wintergreen</i>	Wintergreen.....	Methyl salicylate
<i>Oil bitter almonds</i>	Bitter almonds.....	Benzaldehyde
<i>Cinnamon oil</i>	Cinnamon.....	Cinnamic aldehyde (Eugenole)
<i>Cassia oil</i>	Cassia.....	Cinnamic aldehyde
		Cinnamyl acetate
<i>Anise oil</i>	Anise seed.....	Anethole
		Estragole
		Anis aldehyde
<i>Clove oil</i>	Clove.....	Eugenole
<i>Geranium oil</i>	Geranium.....	Geraniol
		Citronellol
<i>Lemon oil</i> ..	Lemon.....	Limonene
		Phellandrene
		Citral
		Citronellol
		Geraniyl acetate
		Linalol
<i>Orange blossom oil (Neroli)</i>	Orange blossoms.....	Linalol
		Linalyl acetate
		Geraniol
		Methyl anthranilate
		Limonene
<i>Orange oil</i>	Orange rind.....	Limonene
		(Citral Citronellol)
<i>Lemon grass oil</i>	Andropogon citratus..	Citral
<i>Rose oil</i>	Rose.....	Geraniol
		Citronellol
		Geraniyl acetate
<i>Peppermint oil</i>	Peppermint.....	Menthol
		Menthyl esters
		Menthone
		(Pinene, Limonene)
<i>Turpentine oil</i>	Conifers.....	Pinene
<i>Pine needle oil</i>	Pine needles.....	Pinene
		Sylvestrene
<i>Rosemary oil</i>	Rosemary.....	Pinene
		Camphene
		Cineol
		Camphor
		Borneol
<i>Camphor</i>	Camphor tree.....	Camphor
		Borneol
<i>Camphor oil</i>	Camphor tree.....	Pinene
		Phellandrene
		Dipentene
		Eugenole
		Terpineol
		Cineol
<i>Spearmint oil</i>	Spearmint.....	Linalol
		Carvone
<i>Tansy oil</i>	Tansy.....	Thujone
		Camphor
		Borneol
<i>Ylang-ylang</i>		Linalol
		Geraniol
		Benzoic esters
		Methyl ester of p-cresol

Rubber—Caoutchouc

Source.—The common substance which is known as **rubber** is the product obtained by the coagulation of the juice or *latex* which is present, usually in the bark, but sometimes in the woody tissue, of certain tropical or sub-tropical trees, shrubs and vines. **Gutta-percha** is a variety of rubber differing in physical properties. The chemical individual present in rubber is a terpene hydrocarbon known as **caoutchouc**.

Though rubber-yielding plants are quite widely distributed geographically, the chief commercial localities are the Amazon region of South America (*Para rubber*), the Congo region of central Africa, and the Malay peninsula with the adjoining islands. In the Amazon region the trees are native or wild, while in the Malay States cultivation of the trees on large plantations is practiced. When the latex is obtained from the bark it is secured by cutting incisions and allowing the juice to flow out in much the same manner as in the case of turpentine. The latex so obtained is an opaque milky liquid which consists of a water emulsion of globules of pure rubber or caoutchouc. Other substances such as *proteins*, *carbohydrates*, *resins* and *salts* are also present either in solution or suspension.

Coagulation of the Latex.—Pure rubber or **caoutchouc** is an emulsion colloid and in most cases is held in emulsion by the protective action of other colloids, principally proteins. The breaking up of the emulsion with the coagulation of the caoutchouc depends thus upon the removal or destruction of the protective colloids. This is accomplished by different means. The latex of the para rubber from the Amazon is coagulated by heat and smoke, while the latex from the same species of tree on the plantations of the Malay States is usually coagulated by treatment with acid. Boiling of the latex, the addition of formaldehyde, and simple dilution with water are other methods in use. Enzymes are also present associated with the protective colloid proteins but their function seems not to be connected with the coagulation of the caoutchouc.

Properties of Pure Caoutchouc.—Pure caoutchouc may be obtained by dissolving rubber in certain solvents, after first removing resins by solution in acetone. The rubber free from resins is treated with chloroform, benzene, or carbon tetra-chloride, all of which are solvents of caoutchouc. Evaporation of the solvent leaves pure caoutchouc.

Caoutchouc so obtained is a colorless, transparent hydrocarbon of the composition C_8H_8 or better $(C_8H_8)_x$. It is an emulsion colloid of a density approximately 0.90. It is a non-conductor of electricity and this is one of its important properties. It takes up liquids and swells. It is moderately resistant to the diffusion of gases and can be used for balloons but is not as good as other materials. Pure caoutchouc is a soft, sticky, gummy mass of low elasticity and in this condition possesses almost no desirable technical properties. In order to give it such properties it is very definitely changed in the process of manufacture.

Manufacture.—The crude rubber obtained by any of these methods of coagulation contains most of the substances previously mentioned as present in the latex. In the subsequent process of manufacturing rubber goods some of these impurities are partially removed. This is accomplished by macerating the rubber between rolls in the presence of water. The continual maceration and washing removes some of the ash constituents and soluble substances and leaves the rubber in a pure and more uniform condition. During the purification process of maceration and washing the rubber is mixed with certain substances and is then finally subjected to the treatment known as vulcanization. The substances added are of several classes. Metallic oxides such as barium oxide or zinc oxide, barium sulphate (barytes) kaolin, French chalk, are added as fillers to give weight to the rubber. Colored sulphides are added to give color such as the red color of antimony rubber due to **antimony penta-sulphide**. Arsenic and mercury sulphides are also used and likewise red lead (Pb_3O_4) and lead peroxide (PbO_2), lead chromate, Prussian blue and lampblack. The sulphides are effective also in the subsequent vulcanization. Paraffin, rosin and tar are also used. In addition to these are substances added as vulcanizing accelerators, such as litharge (PbO), calcium hydrate and magnesium carbonate.

Vulcanization.—The most important treatment of rubber, in the process of converting it into a technically valuable product, is that known as vulcanization. This consists in the addition of **sulphur** which produces a very definite change in properties. The sticky or adhesive character of pure caoutchouc is entirely lost and it becomes very elastic and does not set when stretched. Even with wide range in temperature it neither hardens nor softens and it becomes insoluble in caoutchouc solvents. The presence of sulphur, usually in small

amounts, thus converts a substance with almost no valuable properties into one of the highest importance in much the same way that the presence of a small amount of carbon changes the properties of pure iron into those of the valuable product known as steel.

As to whether the addition of sulphur is a chemical or physical change we shall say little. Evidence appears on both sides and all we need say here is that, in whichever manner the sulphur really acts, it affects the caoutchouc in a very definite way, is absorbed by it, remains there in some kind of union and is unable to be removed by sulphur solvents. The amount of sulphur thus definitely held by the caoutchouc is about 3 per cent, in the case of soft rubber, while in hard rubber it may be as much as 32 per cent. In both cases more than this amount of sulphur is usually present but the excess is as free sulphur which may be removed by solvents.

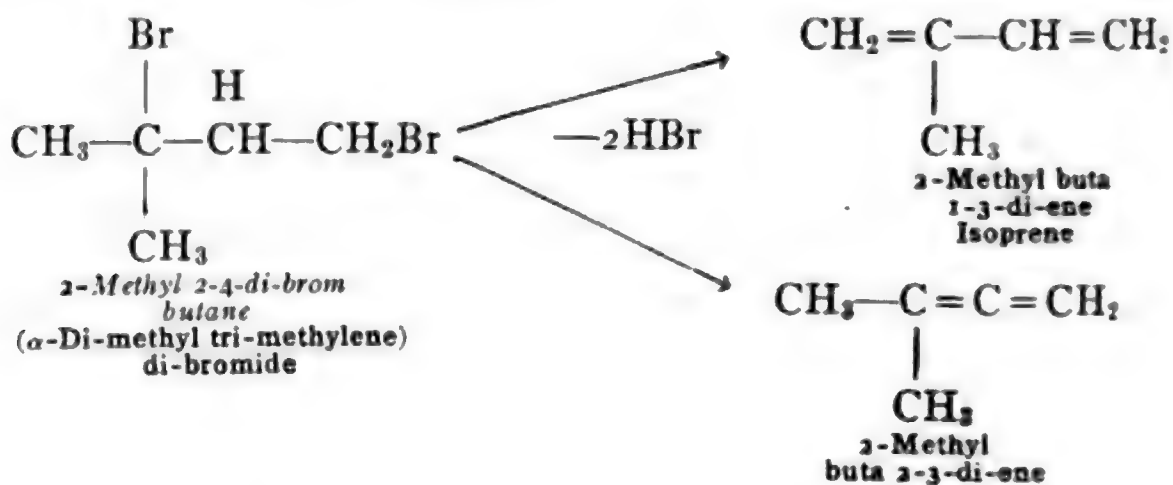
There are two general methods of bringing about this union of sulphur with the caoutchouc. In *hot vulcanization* the sulphur is mixed with the rubber in the process of maceration. The rubber is then subjected to heat, 110° – 140° , by superheated steam in a closed bath or under pressure of heated plates. Still other goods are heated in chambers the temperature of which is raised by means of steam pipes. *Cold vulcanization* is effected by treating the rubber, which has previously had no sulphur mixed with it, with sulphur mono-chloride, (S_2Cl_2), dissolved in carbon disulphide or carbon tetra-chloride. The process of vulcanization was discovered in 1839 by **Goodyear** in the United States and in 1842 by **Hancock** in England, both using the hot process. The cold process was discovered in 1846 by **Parkes**. The important use of rubber technically may be considered as dating from the time of these processes.

Constitution. Synthesis.—The constitution and synthesis of caoutchouc is connected with two of the terpene hydrocarbons previously mentioned. It has been stated that caoutchouc is a hydrocarbon of the composition $(C_5H_8)_x$. As this is the formula for certain of the terpenes we should naturally expect to find that caoutchouc is itself a member of this group.

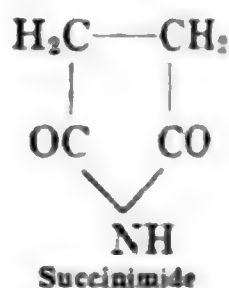
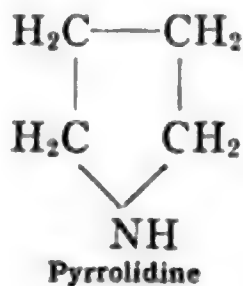
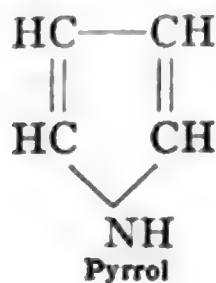
Isoprene.—As early as 1860 it was found that caoutchouc on distillation yielded a terpene hydrocarbon to which the name **isoprene** (p. 162) was given by its discoverer **Williams**, an Englishman. With the isoprene another hydrocarbon was also obtained which was given

different names, viz., *caoutchine* and *di-isoprene*. It was found to be identical with **di-pentene** (p. 819), a terpene obtained from turpentine and which is the inactive form of **limonene**. In 1875 **Bouchardat** converted isoprene into di-pentene and also by distillation, after treatment with hydrochloric acid in the cold, he obtained a residue practically identical with caoutchouc itself. These results were confirmed by **Tilden** in 1882 and in 1884 he obtained isoprene from turpentine. In 1892 **Tilden**, and in 1894 **Weber**, succeeded in obtaining **caoutchouc** from **isoprene** made from turpentine and vulcanized it. Thus far, however, the synthesis of caoutchouc was simply from turpentine, a related substance.

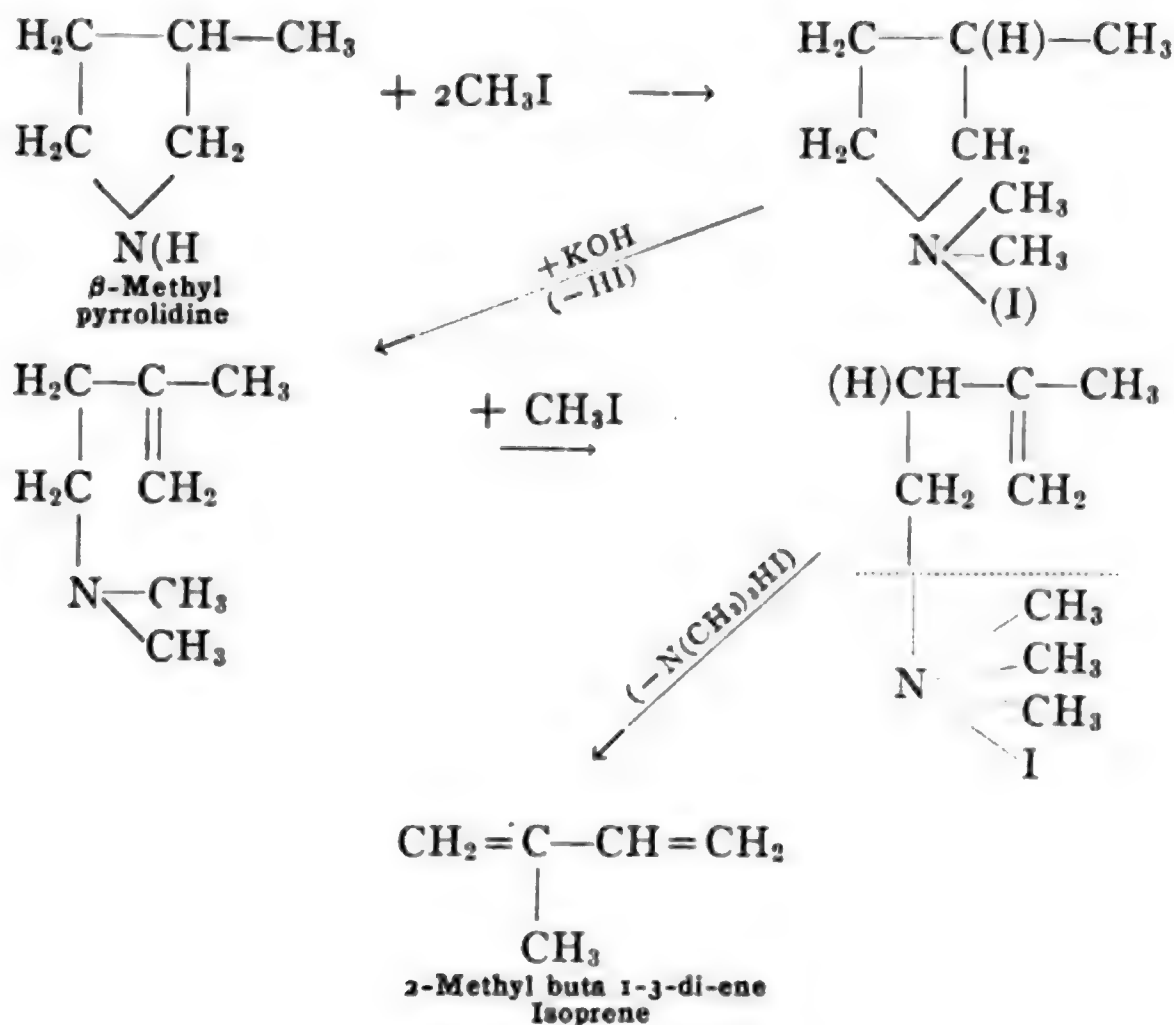
The synthesis of caoutchouc from other compounds than the terpenes themselves was made possible by two syntheses of isoprene which established its constitution. These syntheses were by **Ipatiew** and **Euler** in 1897-98. The synthesis of **Ipatiew** was from **di-methyl tri-methylene di-bromide** or di-brom iso-pentane which is **2-methyl 2-4-di-brom butane**. The reactions are as follows two products being obtained one of which is **isoprene**:



The synthesis of **Euler** started with *beta*-methyl pyrrolidine (p. 854) which is a cyclic imide related to **pyrrol** on one hand and to **succinimide** on the other.



The reactions of the synthesis are



This synthesis proves **isoprene** to be **2-methyl buta 1-3-di-ene**.

While caoutchouc was first obtained by polymerizing isoprene it has been found that other hydrocarbons containing the *buta 1-3-di-ene group* will likewise yield caoutchouc. Such hydrocarbons have been obtained from several sources, *e.g.*, *turpentine*, *petroleum*, *coal*, *acetylene*. Also compounds related to succinic acid, *e.g.*, **pyrotartaric acid** (methyl succinic acid) are possible of transformation into isoprene. **Levulinic acid**, which is **aceto propionic acid**, $\text{CH}_3 - \text{CO} - \text{CH}_2 - \text{CH}_2 - \text{COOH}$, yields a cyclic sulphur compound, **methyl-thiophen** (p. 853), which, like methyl pyrrolidine, yields isoprene. **Ethyl alcohol** by conversion into **acetone** and then by *aldol condensation* with **ethane** yields **2-methyl buta 2-ene**, $\text{CH}_3 - \text{C} = \text{CH} - \text{CH}_3$ which may be transformed



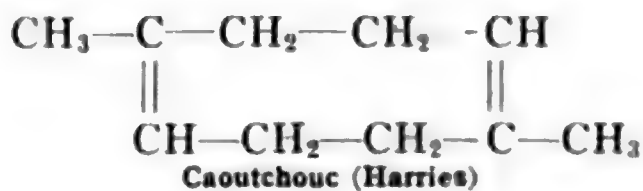
into isoprene. Thus the sources of isoprene and other hydrocarbons which polymerize to caoutchouc include a large variety of substances,

such as carbohydrates, so that the securing of the mother terpene for rubber synthesis is commercially possible.

The polymerization of isoprene to caoutchouc has been accomplished by two general methods: First the production of what is termed *normal caoutchouc* by an auto-polymerization in the presence of acid, alkali, amides, urea, etc. Second, the production of *sodium caoutchouc* by polymerization with sodium or metallic amalgams in the cold or by heat. The different hydrocarbons possible of polymerization to caoutchouc differ as to which of these methods produces the best caoutchouc and also the caoutchouc obtained varies as to its ability to properly vulcanize and yield a satisfactory rubber with proper physical properties.

Thus we may say that while the synthesis of isoprene and other hydrocarbons possible of polymerization into caoutchouc has been definitely accomplished from cheap commercial raw materials, and also the polymerization of these hydrocarbons into caoutchouc has been likewise accomplished, together with the vulcanization of the synthesized caoutchouc, yet the actual production on a commercial scale of a *synthetic rubber* possessing the necessary physical properties for technical use is hardly an accomplished fact at present. This is due, no doubt, largely to the fact that the valuable properties of rubber rest not simply on the chemical constitution of the caoutchouc but, in an even larger degree, on the physical properties of the substance, which, as a colloid, is among those interesting and important substances which we are just beginning to investigate and understand.

In concluding the discussion of rubber it may be well to give without further comment a suggested constitution for caoutchouc itself as a *polymerized isoprene*. The formula suggested by Harries is 1-5-dimethyl cyclo octa di-ene.



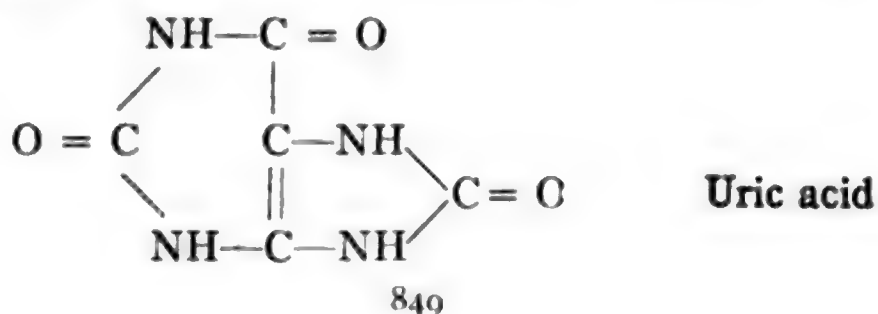
SECTION II

HETERO-CYCLIC COMPOUNDS

In the introduction to the benzene series or carbo-cyclic compounds (p. 458) the group of *hetero-cyclic compounds* was referred to. The representatives of this group which were mentioned at that time were all direct derivatives of the open chain compounds. They included the *lactones*, the *lactams*, the *di-basic acid anhydrides* and the *imides* corresponding to the last, *e.g.*:

$\begin{array}{c} \text{CH}_2\text{---CH}_2\text{---CH}_2\text{---CO} \\ \qquad \qquad \qquad \\ \text{---O---} \end{array}$	Butyro lactone, from γ -hydroxy butyric acid
$\begin{array}{c} \text{CH}_2\text{---CH}_2\text{---CH}_2\text{---CO} \\ \qquad \qquad \qquad \\ \text{---NH---} \end{array}$	Pyrrolidon, lactam of γ -amino butyric acid
$\begin{array}{c} \text{CH}_2\text{---CH}_2\text{---CH}_2\text{---CH}_2\text{---CO} \\ \qquad \qquad \qquad \\ \text{---NH---} \end{array}$	Piperidon, lactam of δ -amino valeric acid
$\begin{array}{c} \text{OC---CH}_2\text{---CH}_2\text{---CO} \\ \qquad \qquad \qquad \\ \text{---O---} \end{array}$	Succinic anhydride
$\begin{array}{c} \text{OC---CH}_2\text{---CH}_2\text{---CO} \\ \qquad \qquad \qquad \\ \text{---NH---} \end{array}$	Succin-imide

All of these are derived from open chain compounds by the loss of water, the ends of the chain being linked together forming a ring, the carbon groups being linked together by an anhydride element or group, *e.g.*, oxygen or the imide group. This ring is *hetero-cyclic* as distinguished from *carbo-cyclic* as in benzene. Also in **uric acid** we have a double hetero-cyclic compound containing two urea groups acting as the ring formers.



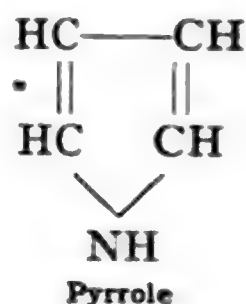
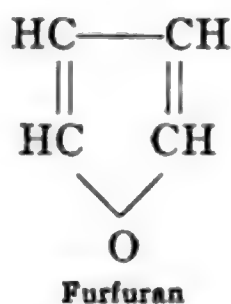
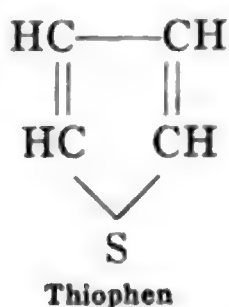
Most of these compounds will not be discussed further as they have been fully treated in connection with the open chain compounds from which they are derived. In all respects they are open chain derivatives.

In addition to these, however, there are several other very important compounds of hetero-cyclic structure which are not so closely related to the open chain compounds and which are better considered now in connection with others, which are in turn directly related to benzene.

Like the carbo-cyclic compounds the hetero-cyclic group is of two types, viz., those containing *one ring* and those containing *two or more condensed rings*. The one ring compounds, furthermore, are of two classes, those containing *five members* in the ring and those containing *six*.

A. FIVE MEMBERED RINGS

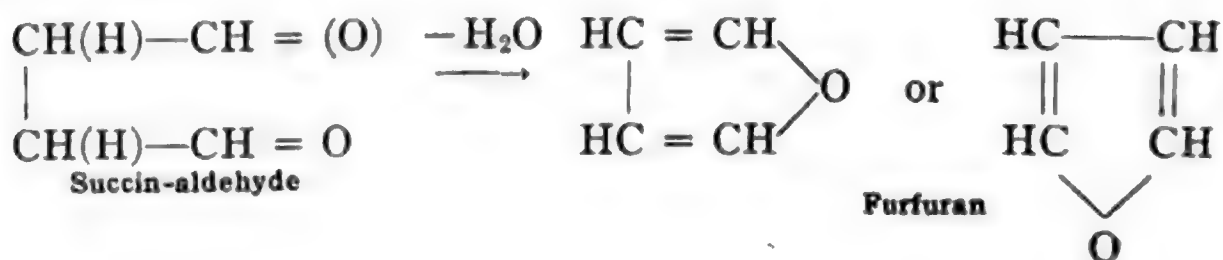
The hetero-cyclic compounds which contain *five members* in the ring are represented by three compounds in one of which *oxygen* is the linking element, in another *sulphur* and in the third the *imide group* (NH). They are as follows:



The constitution of all of these compounds is established by their syntheses from succinic acid.

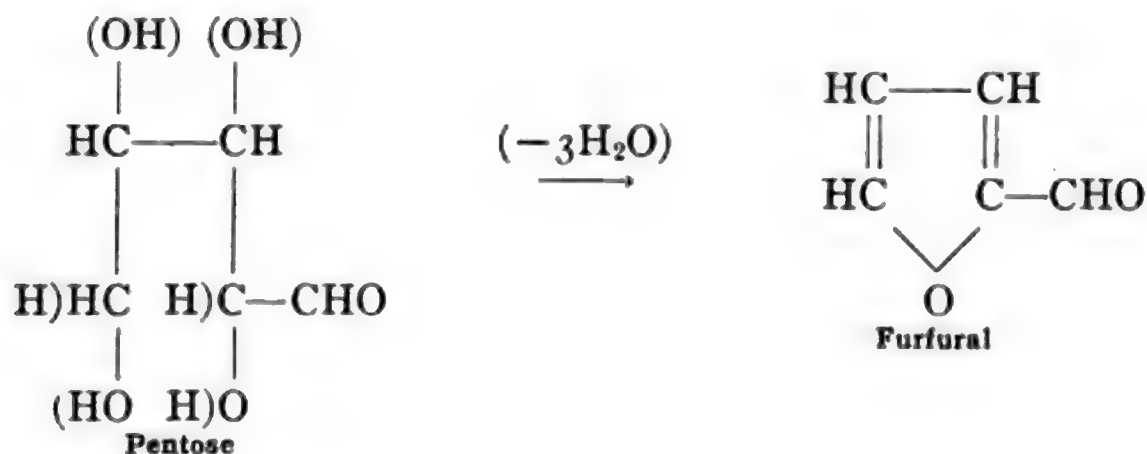
Furfuran, Furfural

When **succin-aldehyde** (di-aldehyde) loses a molecule of water, **furfuran** is obtained, as follows:



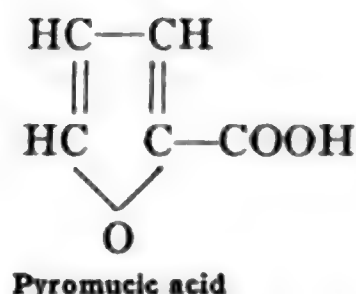
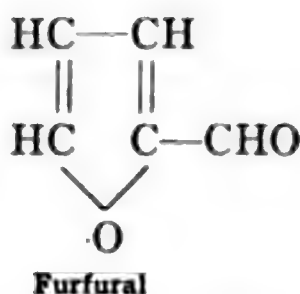
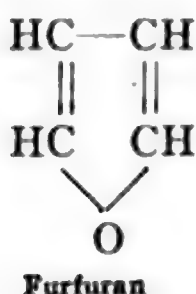
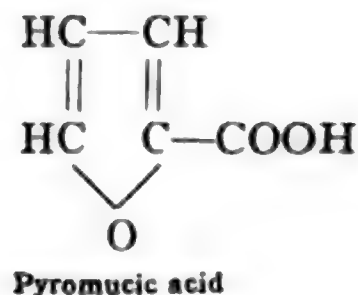
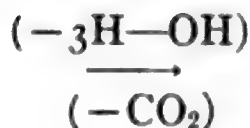
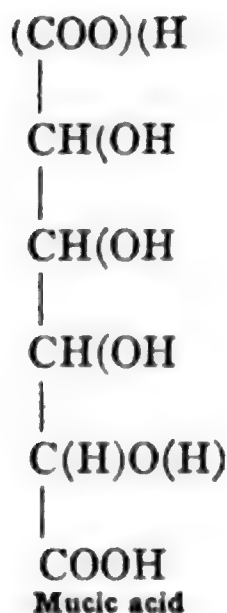
Furfuran, also called **furan**, is a liquid boiling at 32° and is present in *pine tar*. It is not important itself but an aldehyde and an acid derived from it are important.

When pentose sugars, **arabinose** or **xylose** or polypentoses, the *pentosans*, which are present in cereal bran or in most grasses and fodders, are boiled with hydrochloric acid the pentose sugar loses three molecules of water and a product is obtained which proves to be the aldehyde derived from furfuran. This reaction agrees with the constitution as follows:

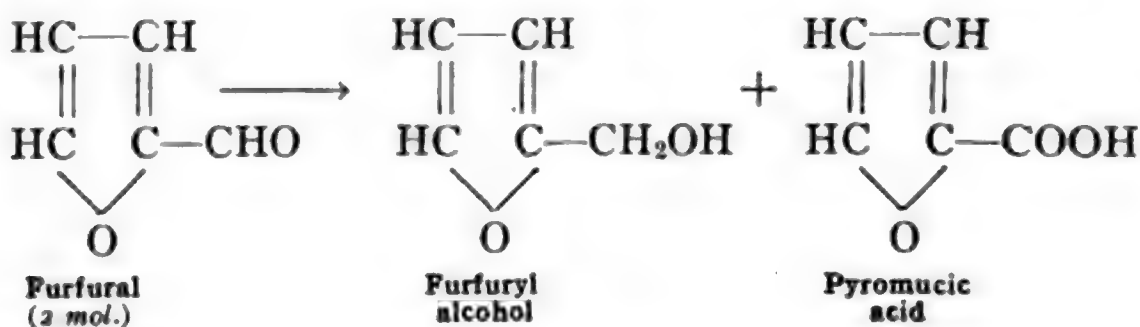


The analytical determination of *pentosans in cattle foods* is based on this formation of **furfural**. The material is boiled under definite conditions with hydrochloric acid and the furfural formed is distilled over. The distillate containing the furfural with water and acid is treated with **phloroglucinol**. On standing a black precipitate of **furfural phloroglucid** is formed. This is filtered, dried and weighed and the amount of furfural or of pentosan present in the original material is calculated by an empirical method. Furfural is a liquid boiling at 162° and shows distinctive aldehyde reactions, being very similar in this respect to benzaldehyde. It undergoes condensation to form **furfuroin** just as benzaldehyde does to form **benzoin** (p. 764). Furfural on oxidation yields an acid, **pyromucic acid**.

Pyromucic Acid.—When **mucic acid** is heated three molecules of water and one of carbon dioxide are lost and a monobasic acid is obtained known as **pyromucic acid**, and this acid by loss of CO_2 goes to **furfuran** thus proving it to be the acid derived from furfuran. The acid is also obtained by oxidizing **furfural**. The reactions and relationships are as follows:



Furfuryl Alcohol.—An alcohol, **furfuryl alcohol**, is also known obtained from the aldehyde by reduction. This reduction is brought about by treatment with alcoholic potassium hydroxide, one molecule of the aldehyde being reduced at the expense of a second molecule which is thereby oxidized to the acid. Thus one molecule of pyromucic acid and one of furfuryl alcohol are obtained from two molecules of furfural.

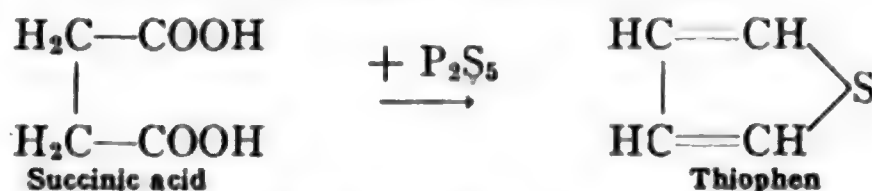


Thiophen

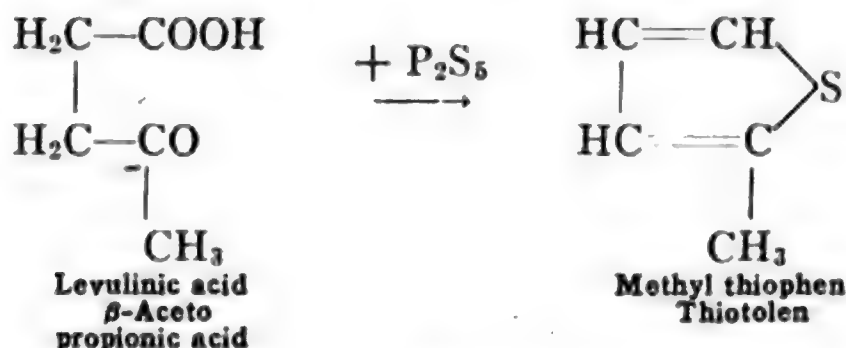
In **thiophen** the oxygen of furfuran is replaced by *sulphur*. Its name indicates its occurrence in crude benzene as obtained from coal tar. Coal tar benzene gives a blue color with **isatin** known as the *indophenin reaction*. This reaction is not given by benzene made from benzoic acid and it was found, by **Victor Meyer**, to be due to the presence

in crude benzene of **thiophen** which he separated by its more easy sulphonation.

The synthesis of thiophen which proves its constitution is from succinic acid by the action of phosphorus penta-sulphide.

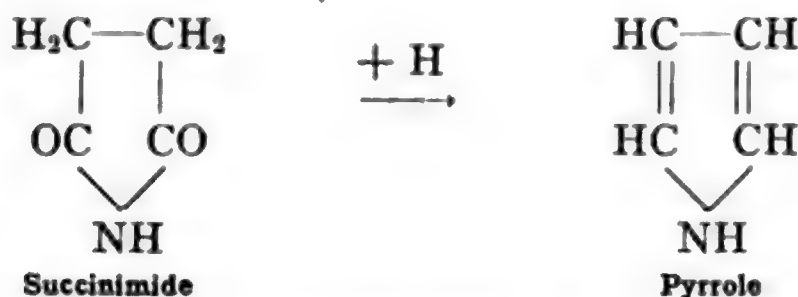


Similarly **levulinic acid**, **aceto-propionic acid**, yields a methyl homologue of thiophen.

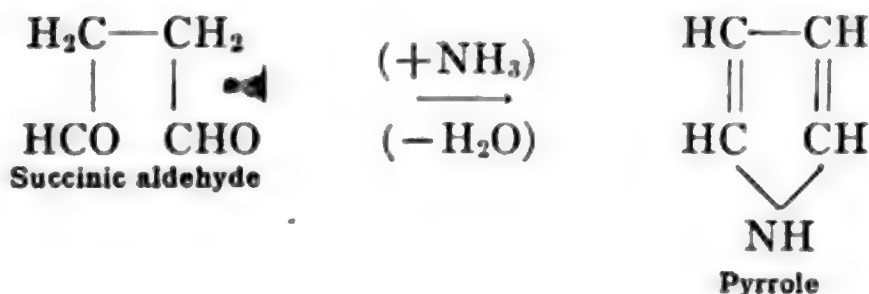


Pyrrole

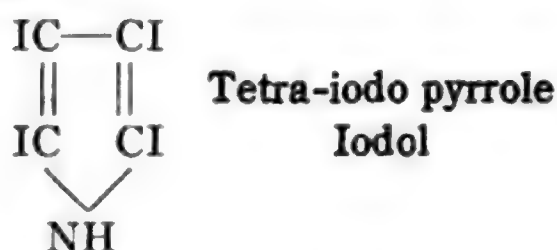
This five membered hetero-cyclic compound is analogous to the two preceding ones having the oxygen of furfuran replaced by the *imide group*, ($-\text{NH}-$). Two methods of synthesis prove its constitution. **Succinimide** when distilled with sodium or zinc dust is reduced and **pyrrole** is obtained.



Similarly succinic aldehyde (di-aldehyde) by treatment with ammonia yields pyrrole.



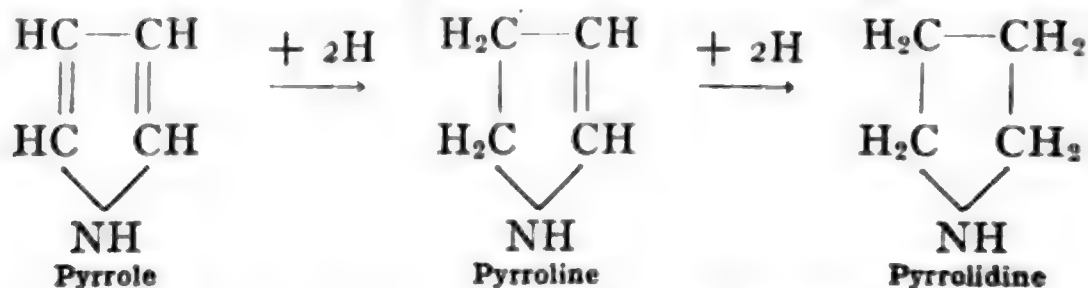
Pyrrole is present in small amounts in coal tar but is obtained in larger amounts from the oil known as *Dippel's oil* which is obtained by distilling bones. It is a colorless liquid boiling at 131° . A characteristic reaction of pyrrole is that a pine shaving moistened with hydrochloric acid is turned a cherry red color by the vapor of pyrrole. This is used as a test for the compound. A striking property of pyrrole is that while it is a weak base, due to presence of the imide group (NH), it likewise acts as an acid, the hydrogen of the imide group being replaced by potassium. This potassium compound by the action of chloroform takes up another carbon and yields a derivative of the corresponding six membered ring compound **pyridine**. It shows its similarity to benzene in forming substitution products, not addition products, with the halogens. The **tetra-iodo pyrrole** is an important anti-septic known as **iodol**.



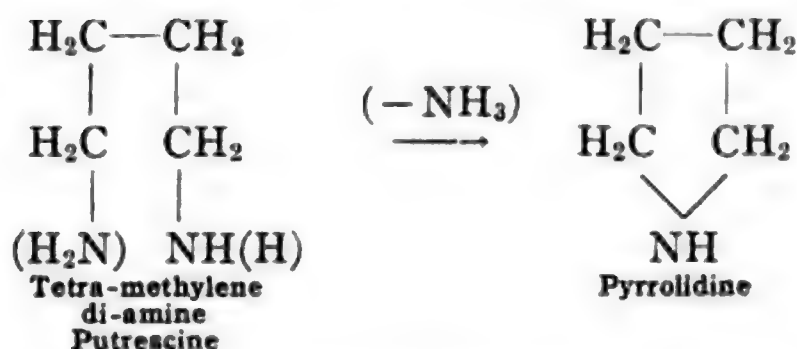
All three of the hetero-cyclic compounds just considered, viz., **furfuran**, **thiophen** and **pyrrole**, possess definite benzene properties. This is as would be expected in the case of compounds containing a carbon cycle with two ethylene groupings. Of the three, thiophen is the most strongly aromatic in its character.

Pyrrolidine

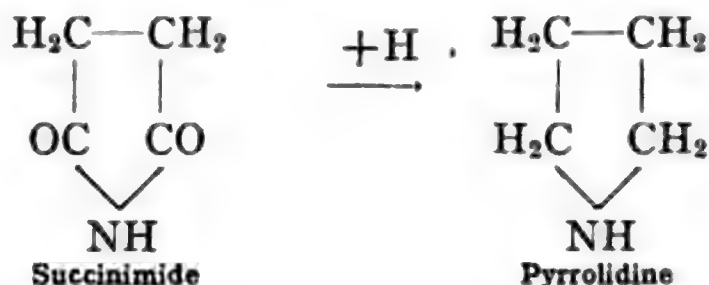
By the action of nascent hydrogen pyrrole takes up two or four hydrogen atoms and is converted into the corresponding hetero-cyclic compounds containing, in the first place, only *one* ethylene group, and in the second *none*, the final compound being fully saturated. The first compound is known as **pyrroline**, the second as **pyrrolidine**.



Pyrrolidine may be synthesized from **tetra-methylene di-amine**, **putrescine** (p. 194), by the loss of ammonia.

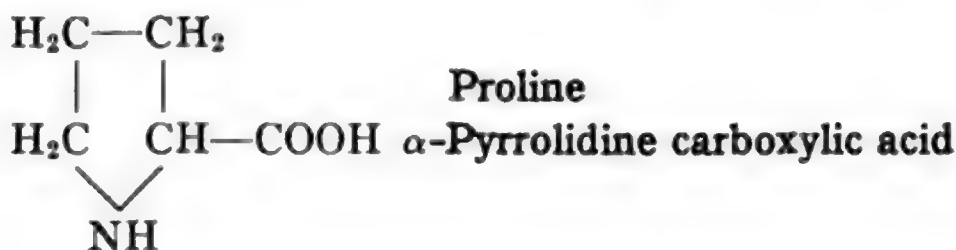


Pyrrolidine is also obtained from **succinimide** by reduction



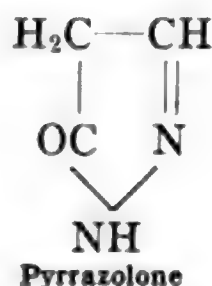
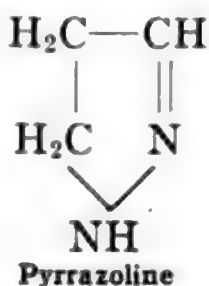
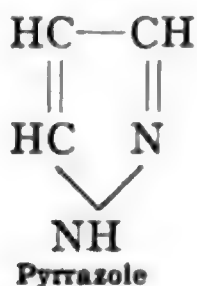
All of these syntheses show clearly the relationship between **pyrrole** and **pyrrolidine** and confirm the constitution of pyrrole and of the other five membered hetero-cyclic compounds.

Proline.—Two of the amino acids obtained as hydrolytic cleavage products of proteins are derivatives of pyrrolidine. They are **proline** and **oxyproline** (p. 392). Proline is *alpha*-pyrrolidine carboxylic acid.

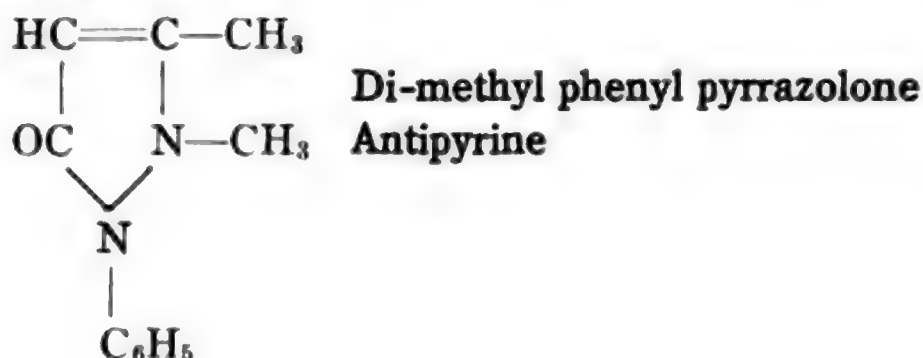


Pyrrazole, Pyrrazoline, Pyrrazolone

When pyrrole and pyrrolidine have one of their CH groups replaced by *nitrogen*, derivatives are obtained known as **pyrrazole** and **pyrrazoline**. Pyrrazoline yields a ketone known as **pyrrazolone**.



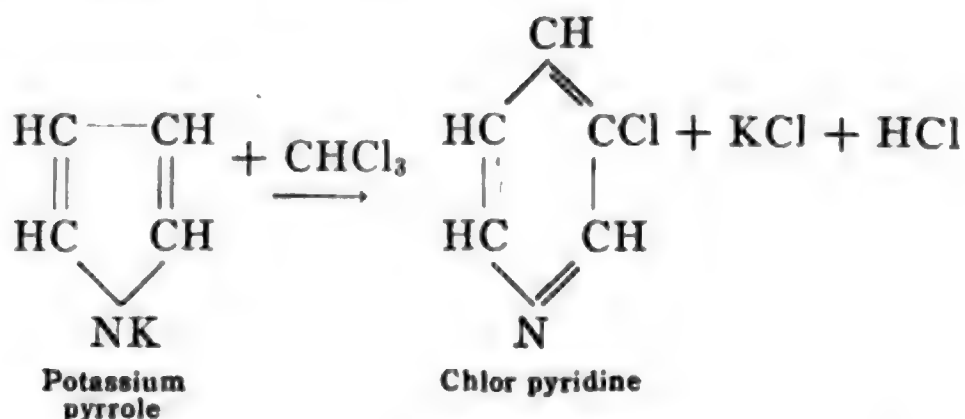
Antipyrine.—A di-methyl phenyl substitution product of pyrrazolone is the important medicinal compound used as a febrifuge and known as **antipyrine**.



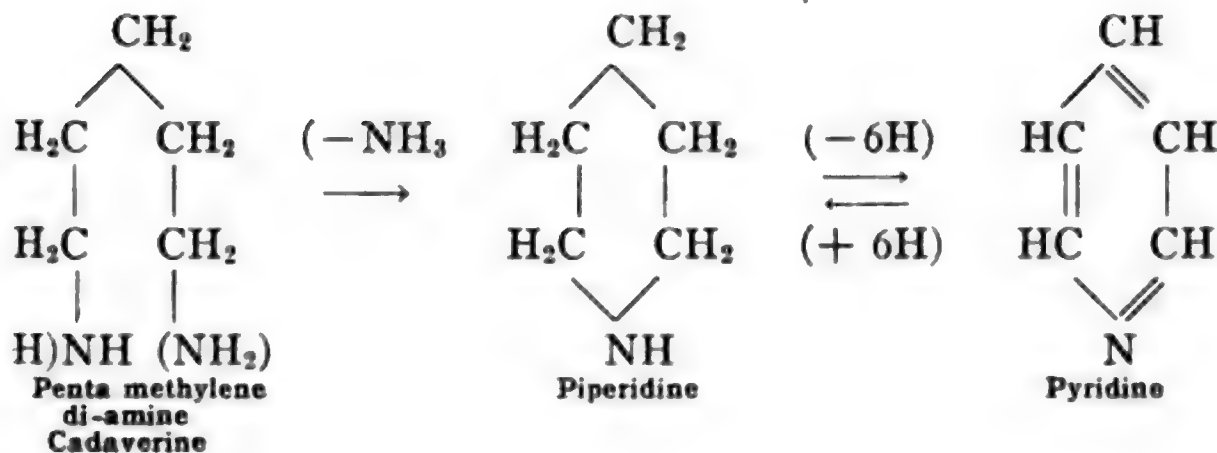
B. SIX MEMBERED RINGS

Pyridine

The only six membered hetero-cyclic compound which we shall consider is the one analogous to pyrrole. It contains a hetero-cyclic ring of five carbons and one nitrogen just as pyrrole contains four carbons and one nitrogen. This compound is known as **pyridine**. That pyridine is a six membered ring analogous to pyrrole is proven by the fact previously referred to (p. 854), that potassium pyrrole by the action of chloroform takes up an additional carbon and yields a chlorine substitution product of pyridine.

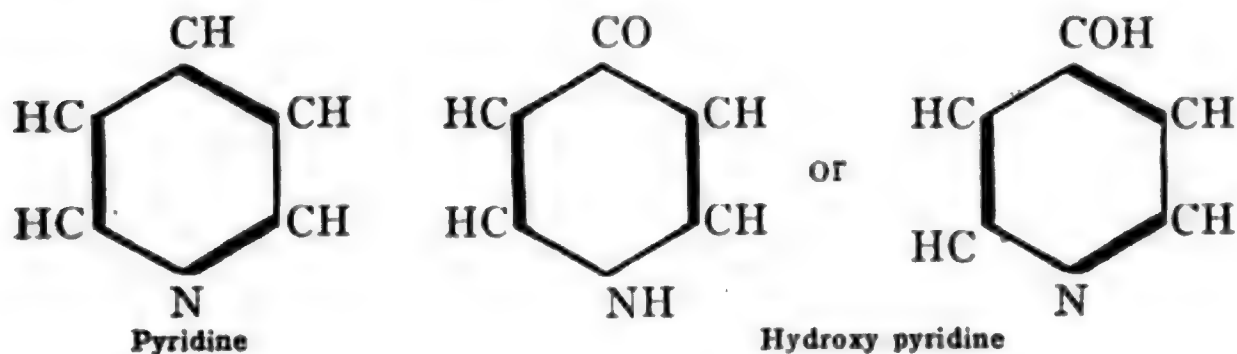


The constitution of pyridine is established by numerous syntheses. The only one we shall mention is the one from **cadaverine** or **penta-methylene di-amine**. The corresponding tetra-methylene di-amine, as already stated (p. 855), loses ammonia and yields pyrrolidine, the saturated hydrogenated pyrrole. By an exactly similar reaction penta-methylene di-amine loses ammonia and yields the saturated hydrogenated pyridine which is known as **piperidine**.



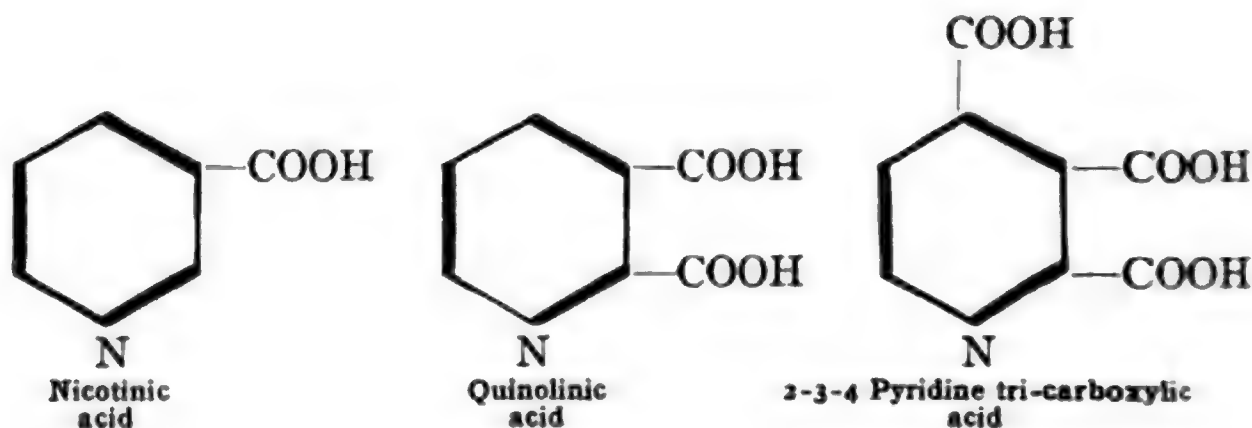
Piperidine by loss of six hydrogens yields **pyridine** and is similarly made from pyridine by addition of six hydrogens. Pyridine may be considered, therefore, as benzene in which one carbon group is replaced by nitrogen. In its reaction and properties pyridine shows its similarity to benzene. It acts as a tertiary base and like benzene may be chlorinated or sulphonated, though not as easily. It is a colorless liquid boiling at 115° , mixing with water, and possessing a strong characteristic odor. On this account it is used in its crude form, mixed with related compounds, as a denaturant of alcohol. Pyridine is found in coal tar and is separated from benzene and other constituents of light oil by treatment with sulphuric acid which forms the sulphate. It is also present in *bone oil* (*Dippel's oil*) together with pyrrole.

Derivatives of Pyridine.—(1) *Hydroxy pyridines*. These compounds may be considered as ketone derivatives of a di-hydro pyridine or as hydroxyl derivatives of pyridine. The two tautomeric formulas thus represent them as follows:



(2) *Carboxylic acids*. Of these pyridine acids there are mono-, di-, and tri-carboxylic acids known, which are obtained by oxidation of the corresponding mono-, di-, and tri-methyl homologues. One of the mono-carboxylic acids is known as **nicotinic acid** and is obtained

by oxidizing **nicotine**, the alkaloid of *tobacco*. The 2-3-di-carboxylic acid is known as **quinolinic acid** and is obtained by oxidizing **quinoline** (p. 862). A tri-carboxylic acid known as **2-3-4 pyridine tri-carboxylic acid** is obtained by oxidizing **cinchonine** alkaloids.



Piperidine

This compound, the *hexa-hydro pyridine*, has just been referred to, and also previously, in connection with **penta-methylene di-amine** (p. 194). In both these connections its constitution has been established. As its name indicates, it is obtained from *pepper* in which it is present in amide combination with an acid known as **piperic acid**. The compound thus formed is the alkaloid of black pepper and is called **piperine**.

Pyridine Homologues

Pyridine yields methyl substitution products which bear the same relationship to it that toluene, xylene and mesitylene do to benzene. These homologues like those of benzene are easily oxidized and yield corresponding carboxyl derivatives or acids, viz., **pyridine carboxylic acids**, as just discussed.

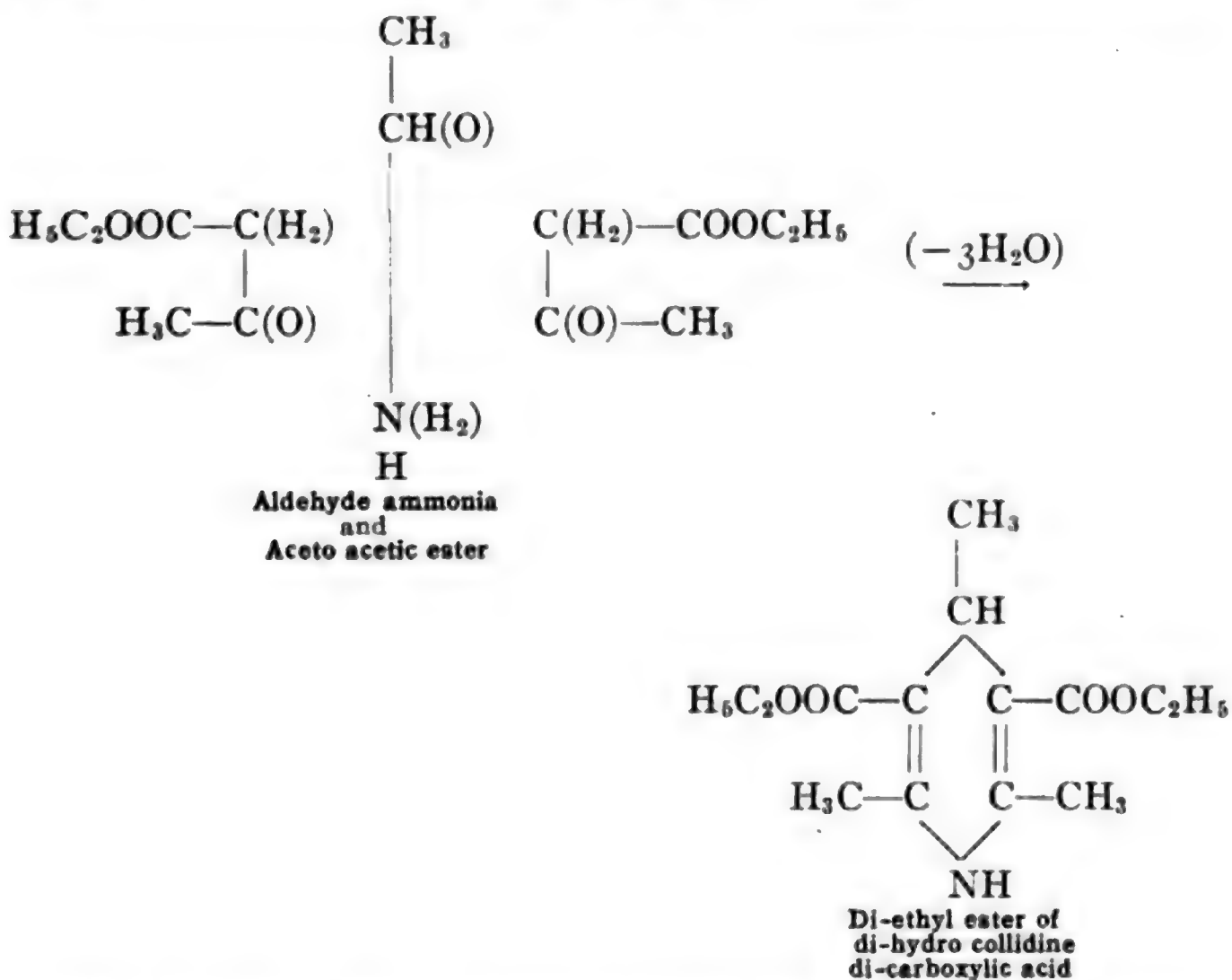
Picolines.—The three isomeric *mono-methyl pyridines* are known as **picolines**. One of these is obtained by heating **strychnine** with lime. From them by oxidation pyridine mono-carboxylic acids are obtained (p. 857).

Lutidines. Collidines.—The *di-methyl pyridines* are known as **lutidines** and the *tri-methyl pyridines* as **collidines**.

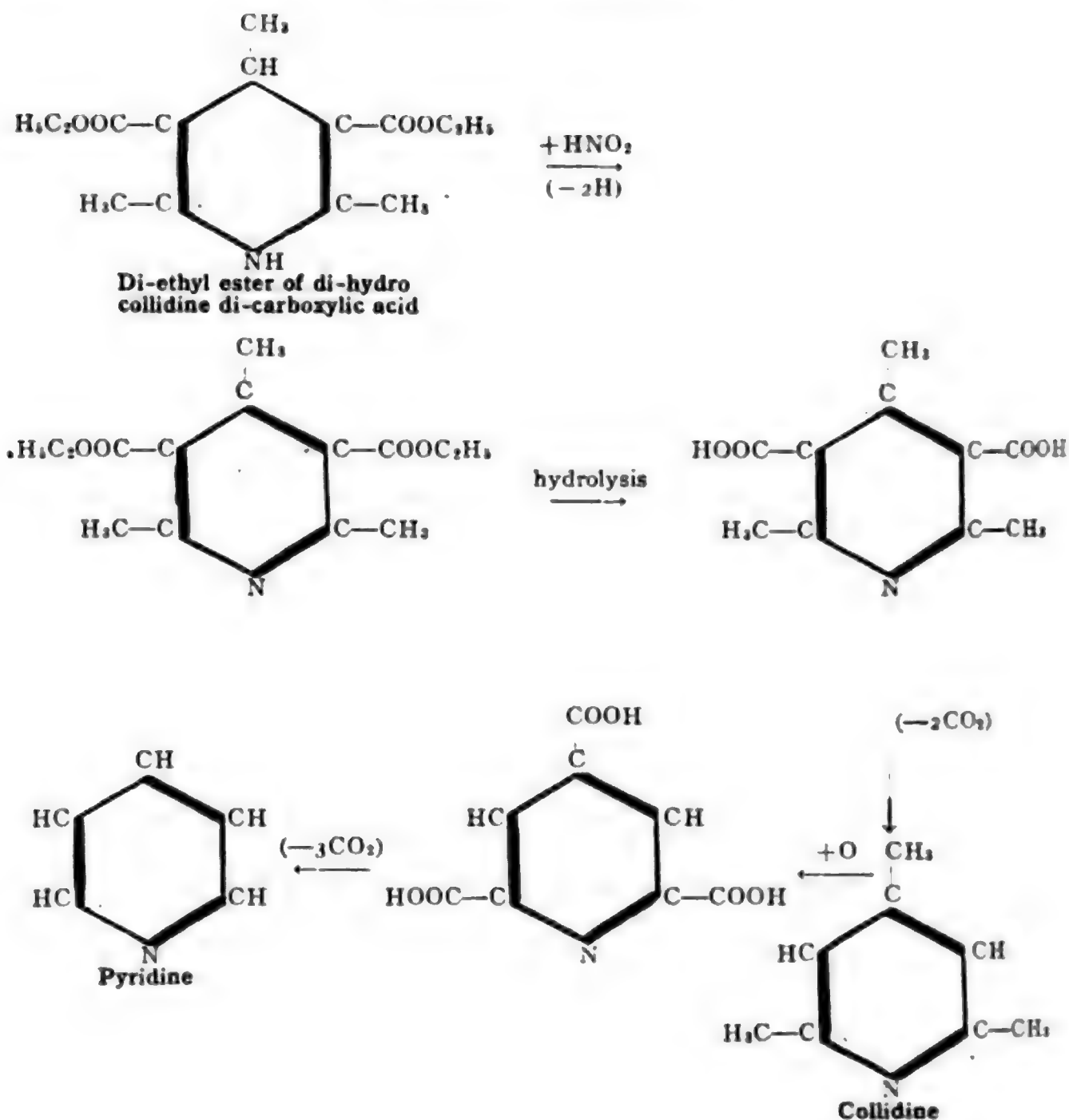
Conine.—One of the most important homologues is, *alpha*-propyl pyridine, which, by hydrogenation, yields *alpha*-propyl piperidine

which is the alkaloid **conine**, the poisonous constituent of *hemlock*. The syntheses of these methyl pyridines are important in establishing their constitution and through them the constitution of pyridine itself. **beta-Methyl pyridine** is obtained by distilling **acrylic aldehyde ammonia**. This explains the occurrence of pyridine in bone oil which is obtained by distilling bones that still have fat on them, the fat yielding acrylic aldehyde or acrolein.

Synthesis of Collidine.—The most important synthesis of pyridine homologues is that of **collidine** from which pyridine may be obtained by elimination of the methyl groups by oxidation and loss of carbon dioxide. When **aldehyde ammonia** is heated with **aceto-acetic ester** a derivative of a *di-hydrogenated collidine* is obtained, as follows:



This di-ethyl ester of di-hydro collidine di-carboxylic acid is then treated with nitrous acid which removes the two added hydrogens. The ester is then hydrolyzed and carbon dioxide eliminated whereby **collidine** is obtained. This, by oxidation of the methyl groups to **carboxyl** groups and elimination of carbon dioxide, yields **pyridine**.



C. CONDENSED HETERO-CYCLIC COMPOUNDS

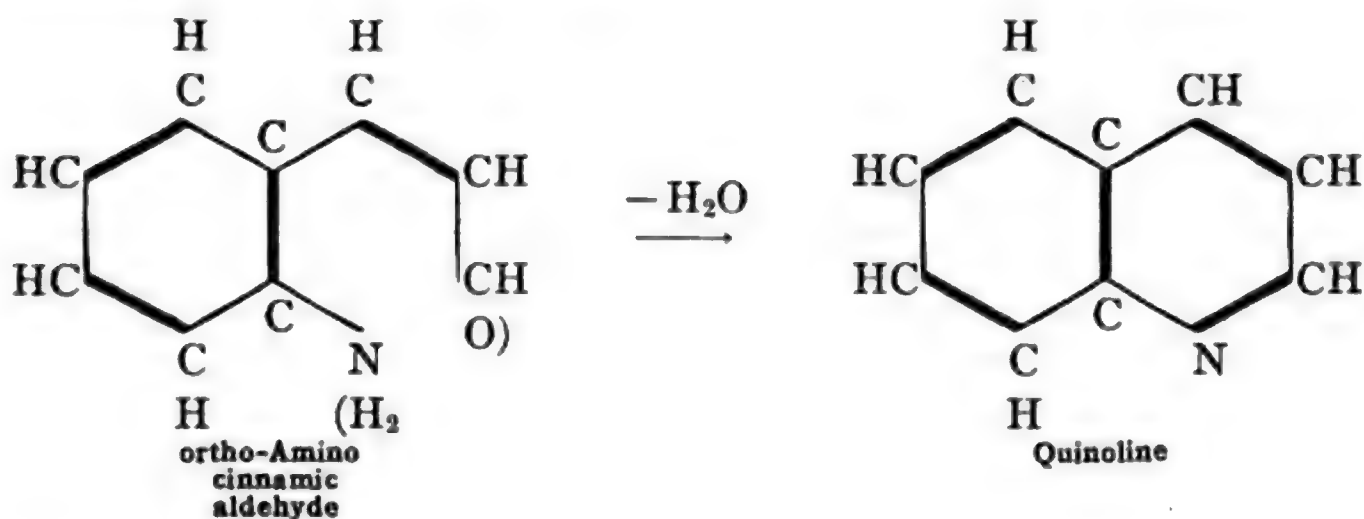
The compounds of this class include those in which *two rings are condensed together* as in naphthalene. They differ from the latter, however, in that one of the rings is *hetero-cyclic*. This hetero-cyclic ring, with which the benzene ring is condensed, may be either a five membered ring, like **pyrrole**, or a six membered ring, like **pyridine**. The compounds which contain a five membered ring include **indigo** and related compounds. Those which contain a six membered ring are represented by a compound known as **quinoline**. Because of the close relationship between this last compound and **pyridine**, which we have just been discussing, it is best to consider it first and indigo later.

CONDENSED SIX MEMBERED HETERO-CYCLIC COMPOUNDS

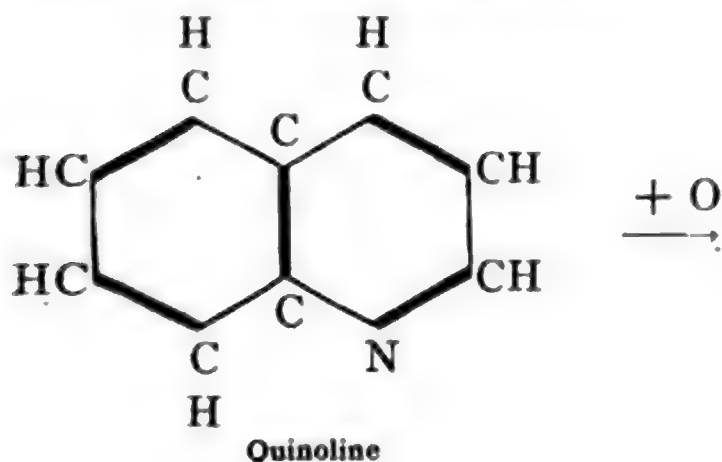
Quinoline

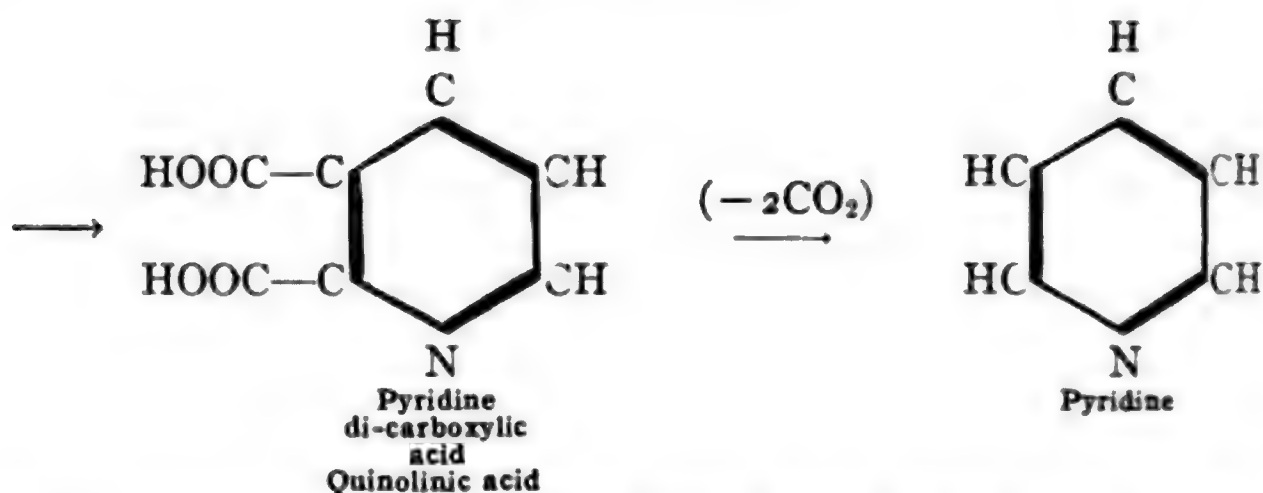
That the constitution of quinoline is that of a condensed ring compound made up of a *benzene ring coupled with a pyridine ring* is shown by its synthesis and its relation to pyridine.

Baeyer and Drewsen's Synthesis.—The synthesis of **Baeyer and Drewsen** shows the constitution the most clearly. **Cinnamic aldehyde** (p. 656) is $C_6H_5-CH=CH-CHO$. When the *ortho-nitro* substitution product of this compound is reduced we obtain the corresponding *ortho-amino cinnamic aldehyde*. This by loss of water yields **quinoline**.



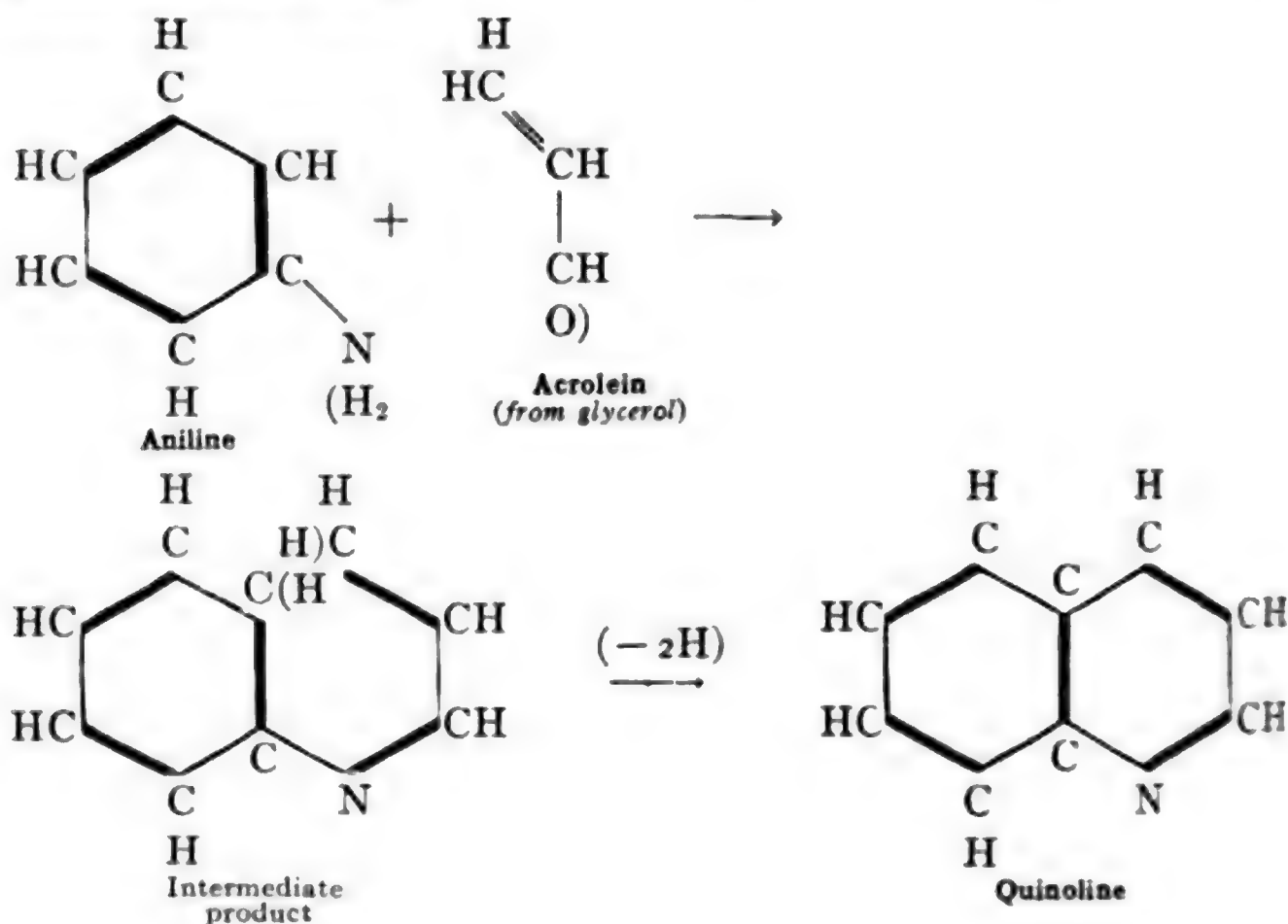
This proves that the end of a propene three carbon side chain is linked to the *ortho* position of a benzene ring by means of nitrogen thereby forming a hetero-cyclic ring coupled to the benzene. That this hetero-cyclic ring is pyridine is proven by the fact that when quinoline is oxidized an *alpha-beta-di-carboxy pyridine* is obtained which by loss of carbon dioxide yields **pyridine**.





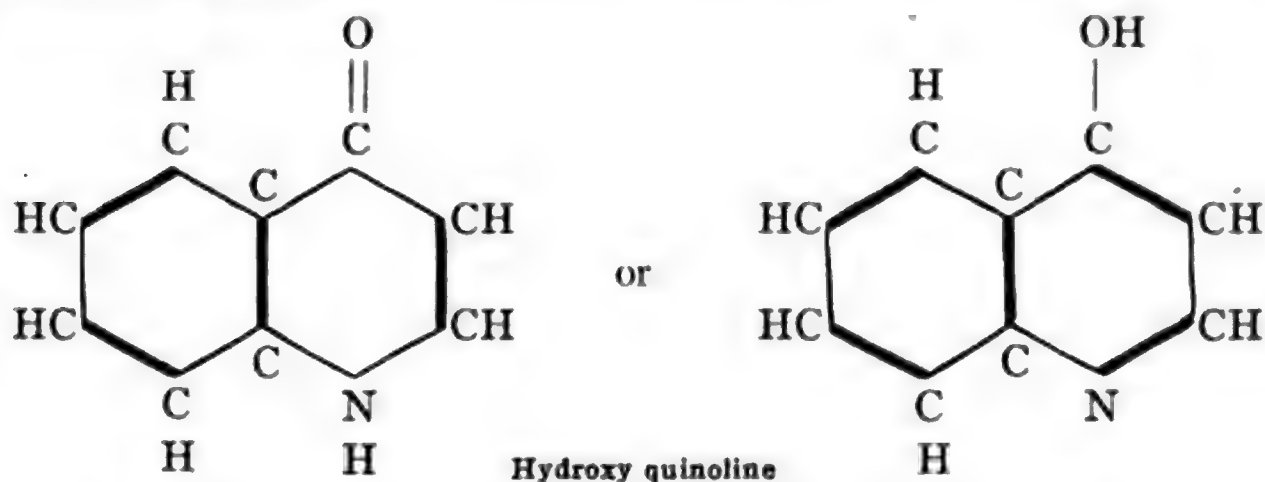
This is exactly analogous to the oxidation of naphthalene to *ortho*-phthalic acid and the conversion of this into benzene (p. 689).

Skraup's Synthesis.—While the synthesis of **Baeyer** and **Drewsen** is the clearest proof of the constitution of quinoline it is not the one most commonly used. The synthesis most frequently associated with the preparation of this compound is that of **Skraup**. This consists in heating together **aniline**, **glycerol** and sulphuric acid in the presence of an oxidizing agent, *e.g.*, nitro benzene or arsenic acid. The glycerol heated with sulphuric acid loses water yielding acrolein or **acrylic aldehyde**. This condenses with the aniline yielding an intermediate product which then by oxidation loses two hydrogens and yields **quinoline**, as follows:

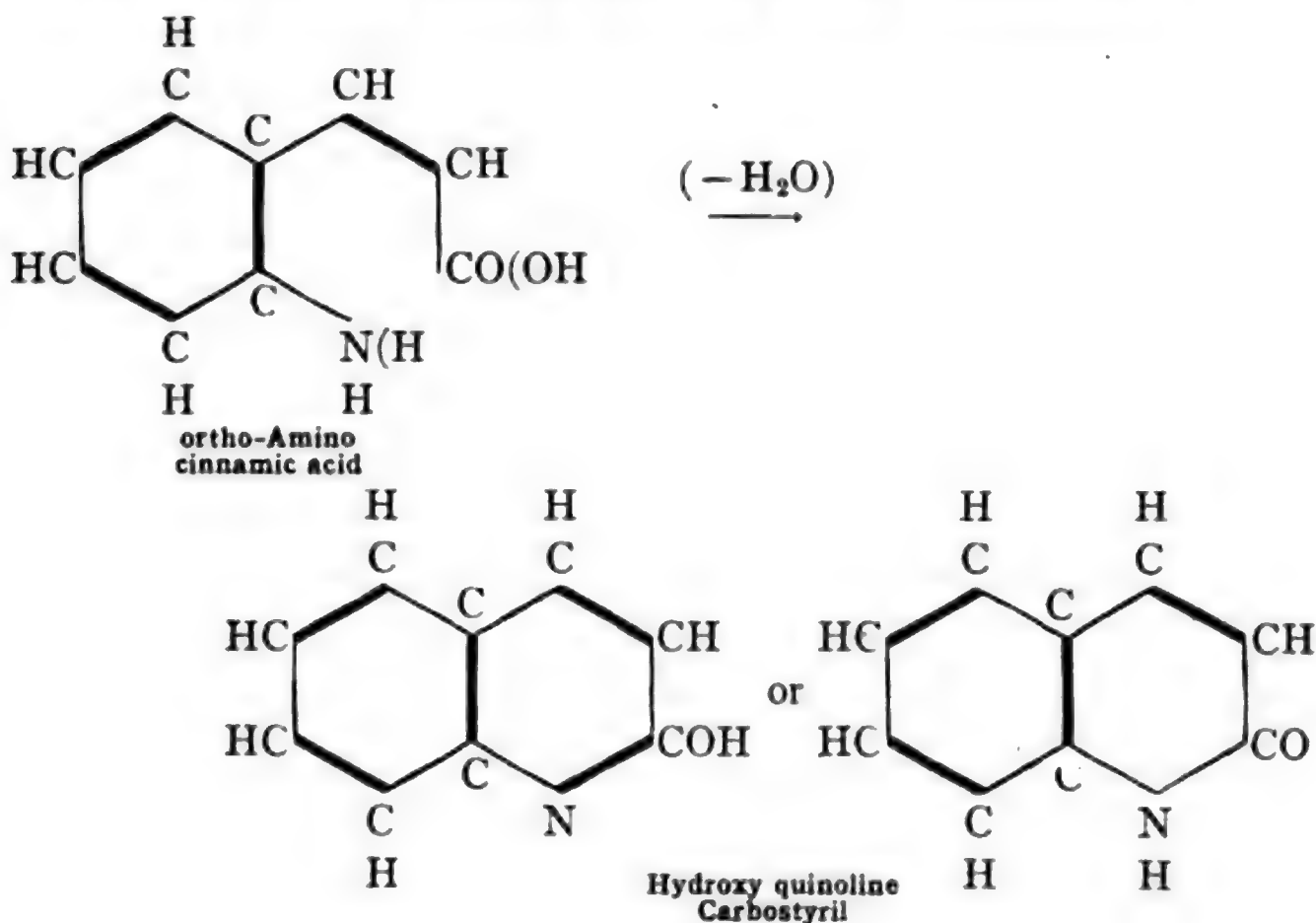


Quinoline is a colorless liquid, b.p. 239° , with a characteristic odor. It possesses the properties of a tertiary amine base forming salts as pyridine does. It is present with the latter in coal tar and in bone oil but is usually not obtained from these sources being prepared by **Skraup's synthesis**.

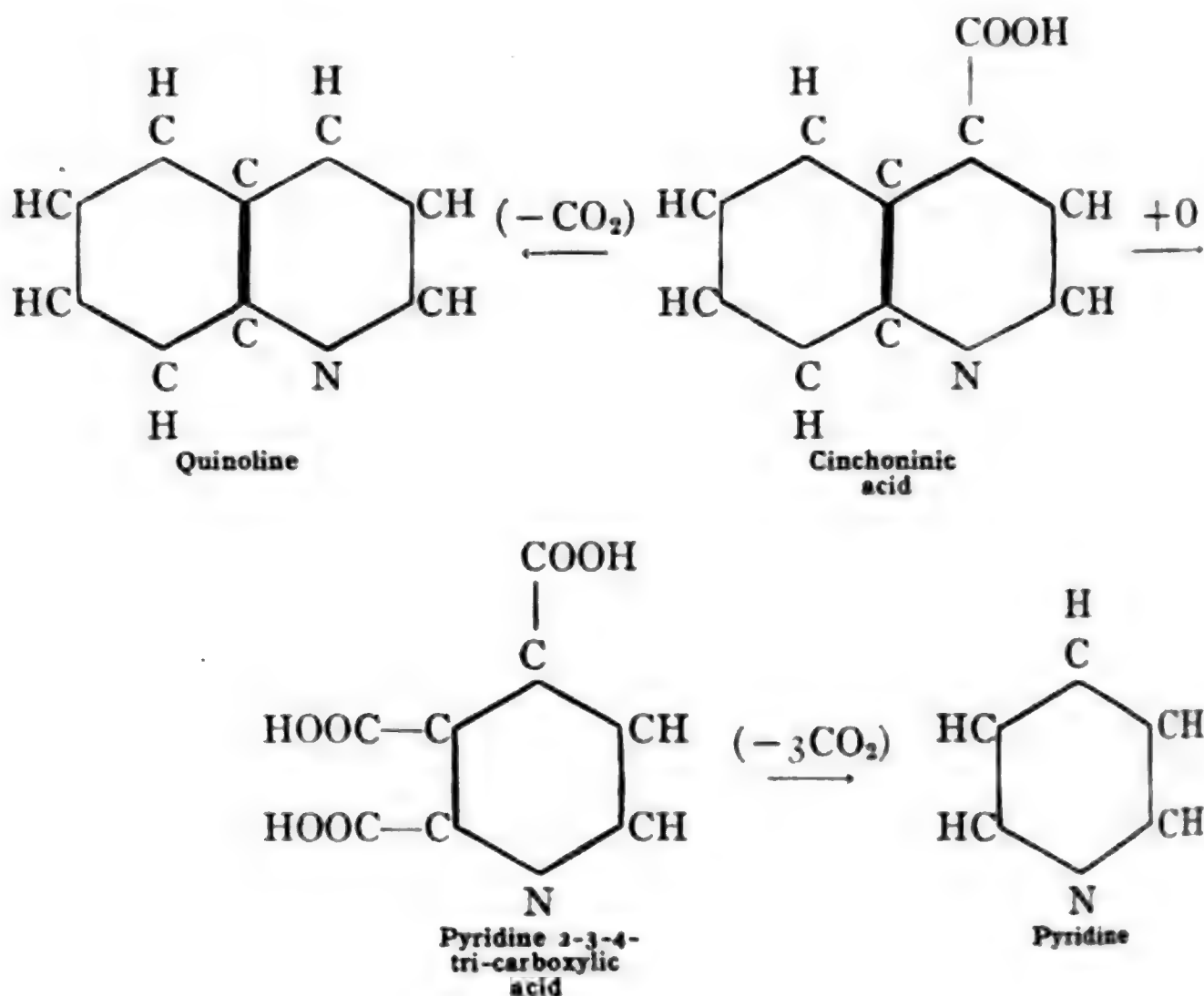
Derivatives of Quinoline.—(1) **Hydroxy quinolines.** These are exactly analogous to the hydroxy pyridines and like them are assigned tautomeric formulas.



Carbostyryl.—If in the **Baeyer and Drewsen** synthesis cinnamic acid is used instead of cinnamic aldehyde the *ortho*-amino derivative, by loss of water, yields a hydroxy quinoline known as **carbostyryl**.

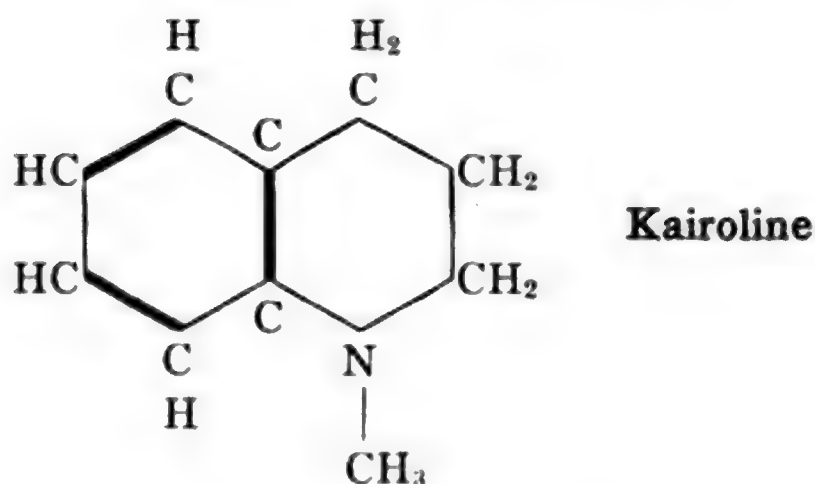


Cinchoninic Acid.—(2) **Carboxylic acids.** The only quinoline carboxylic acid of importance is known as **cinchoninic acid** because it is obtained by oxidizing **cinchonine**, one of the alkaloids of **cinchona bark**. It is the **quinoline 4-carboxylic acid** and by loss of carbon dioxide yields **quinoline**. By oxidation cinchoninic acid yields **pyridine 2-3-4-tricarboxylic acid** (p. 858) which by loss of carbon dioxide (3 mol.) yields **pyridine**.

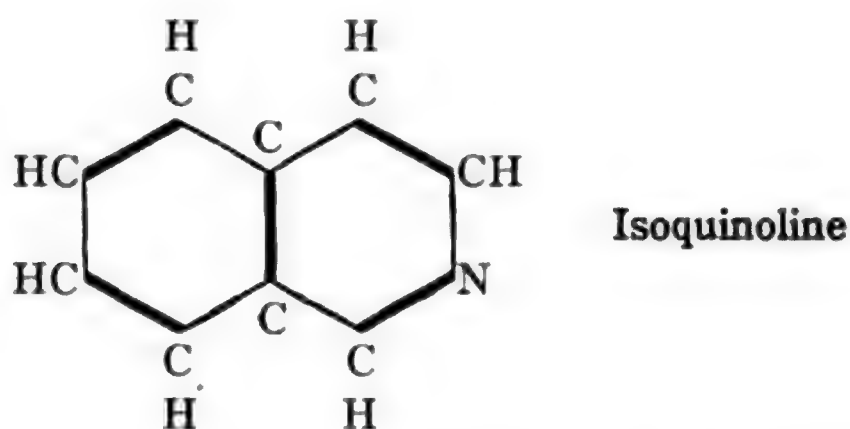


Quinolinic Acid.—This acid which is obtained by oxidizing quinoline is a di-carboxyl pyridine (p. 858, 862).

(3) **Hydrogenated quinolines.** The hydrogenated quinolines which are analogous to **piperidine**, the hydrogenated pyridine, are also known. The methyl amino and ethyl amino derivatives of tetra-hydro quinoline are known as **kairolines** and are *antipyretics*. They exert a toxic action on the blood corpuscles and are therefore not used in medicine.



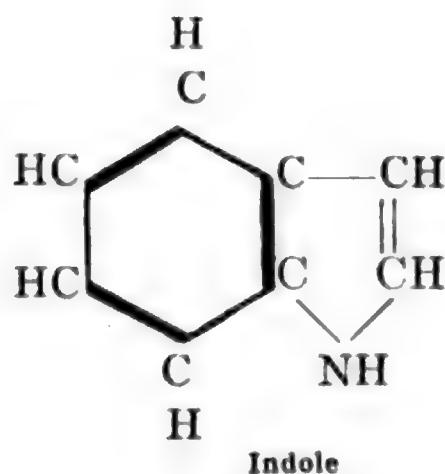
The homologues of quinoline are not important. An isomeric quinoline known as **isoquinoline** has the nitrogen in the *beta* position of the second ring.



soquinoline is of importance in its relation to the alkaloids.

CONDENSED FIVE MEMBERED HETERO-CYCLIC COMPOUNDS

Two of the five membered hetero-cyclic compounds form condensed rings with benzene, viz., **furfuran** and **pyrrole**. The resulting compounds are represented as follows:

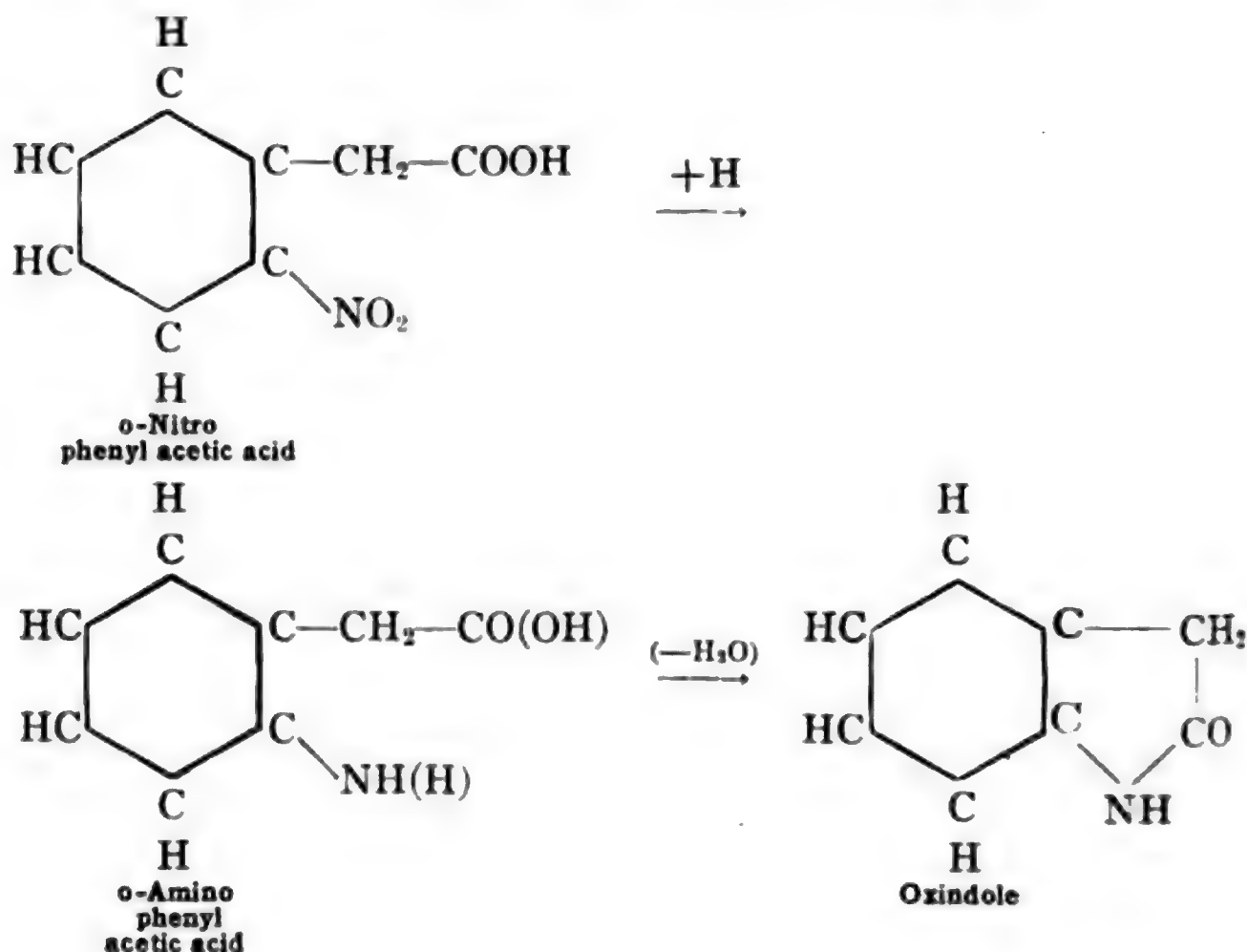


The first compound, a condensed benzene and furfuran, is known as **cumarone** and is present in *cumarone resin*. It is not of special importance.

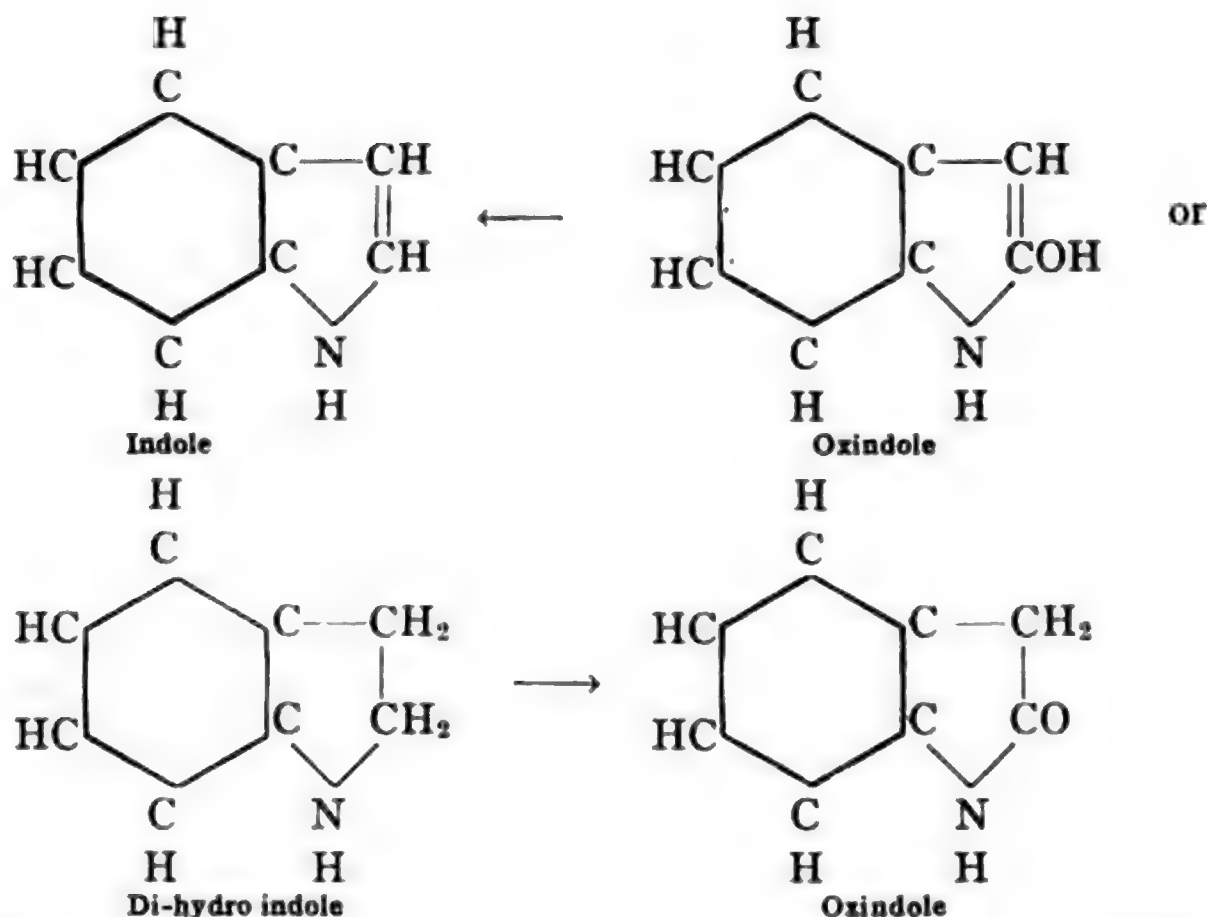
Indole, Oxindole, Di-oxindole, Isatin, Indoxyl

Indole.—The second compound above, a condensed benzene and pyrrole compound, is known as **indole** and is a very important compound both physiologically and in its relation to **indigo**. While indigo itself is not a simple condensed hetero-cyclic compound it belongs here in our discussion because of its relation to indole. The constitution of indole is proven by several synthetic relationships.

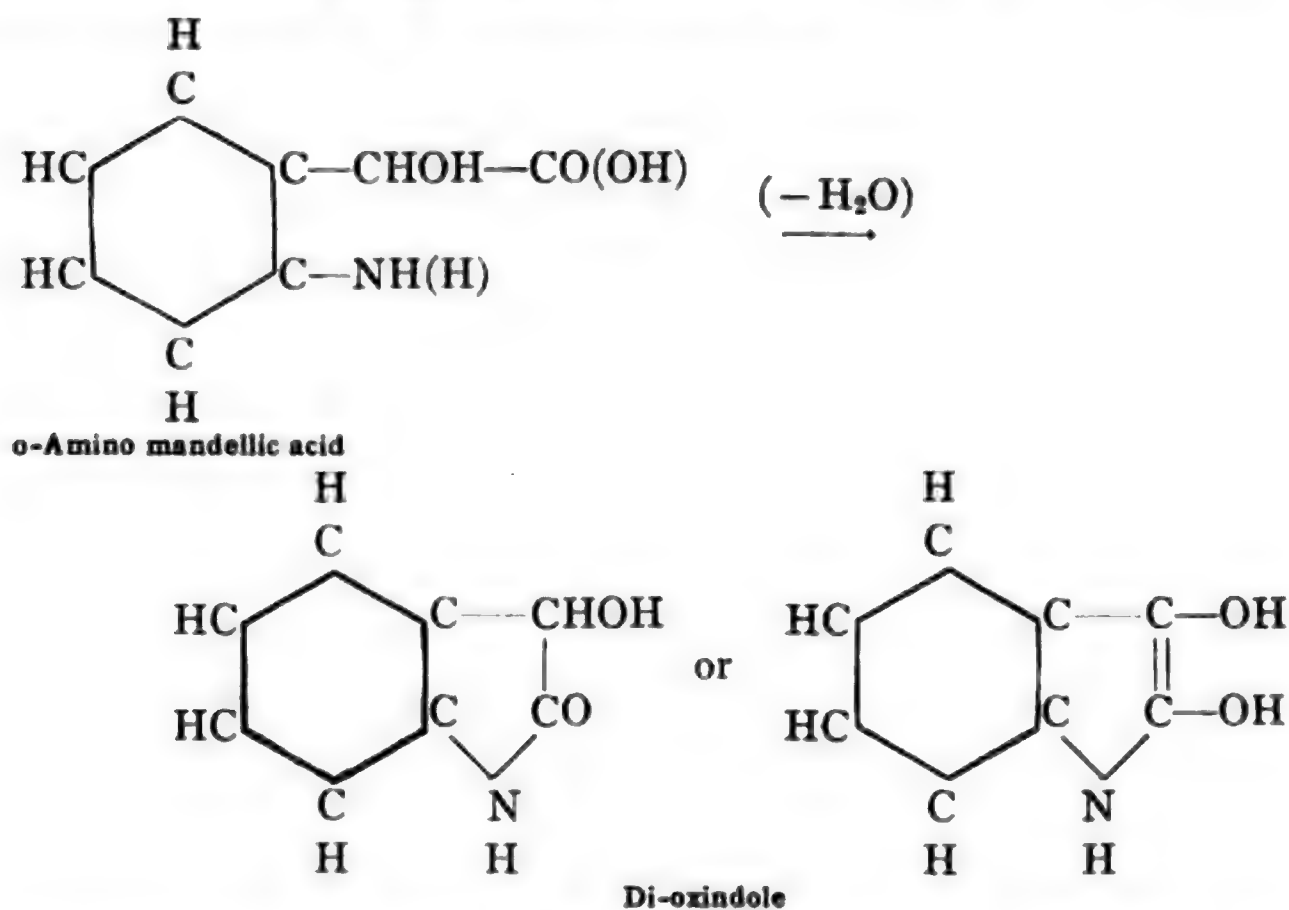
Oxindole.—When **ortho-nitro phenyl acetic acid** is reduced to the **ortho-amino phenyl acetic acid**, the latter, being a *gamma*-amino acid, loses water yielding a *lactam* which is known as **oxindole**.



Now oxindole by reduction with zinc dust yields indole which must therefore have the constitution as given below. Oxindole is the *ketone* of a di-hydrogenated indole, or it may be considered as the tautomeric compound, *i.e.*, a *mono-hydroxy* indole.

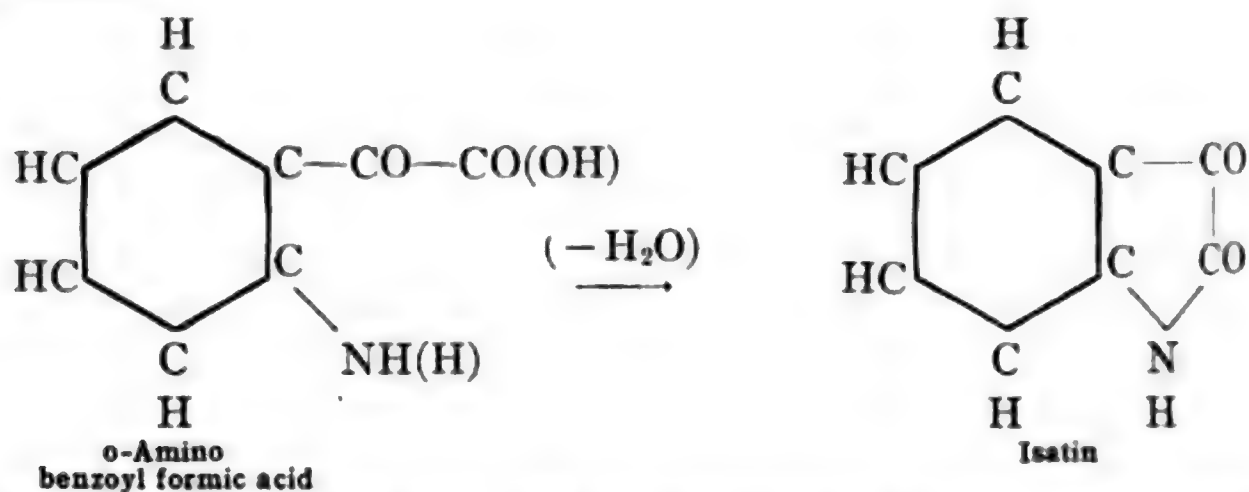


Di-oxindole.—Similarly a di-hydroxy compound known as **di-oxindole** is obtained as a lactam anhydride from **ortho-amino mandelic acid**, **ortho-amino phenyl hydroxy acetic acid**.

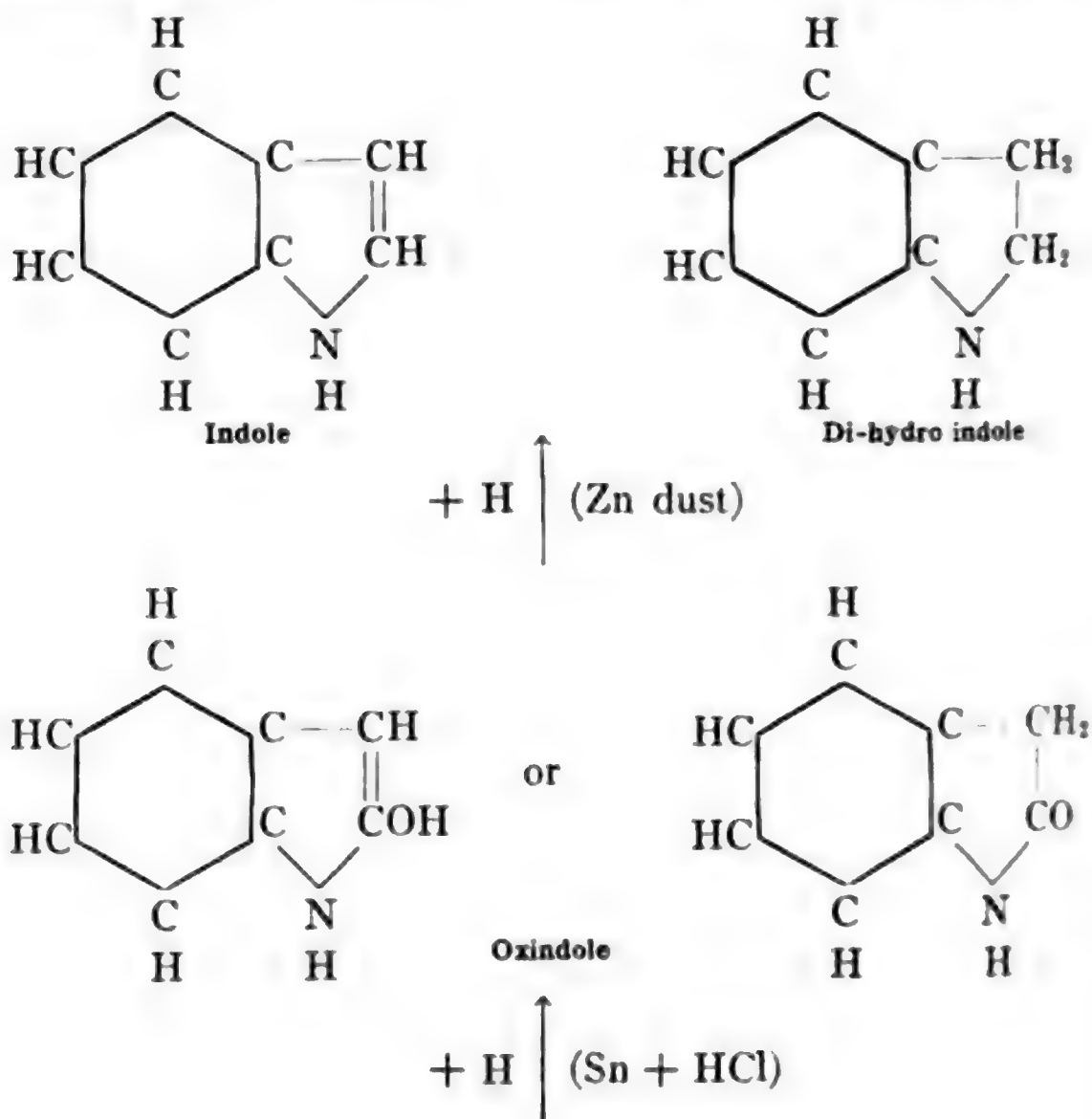


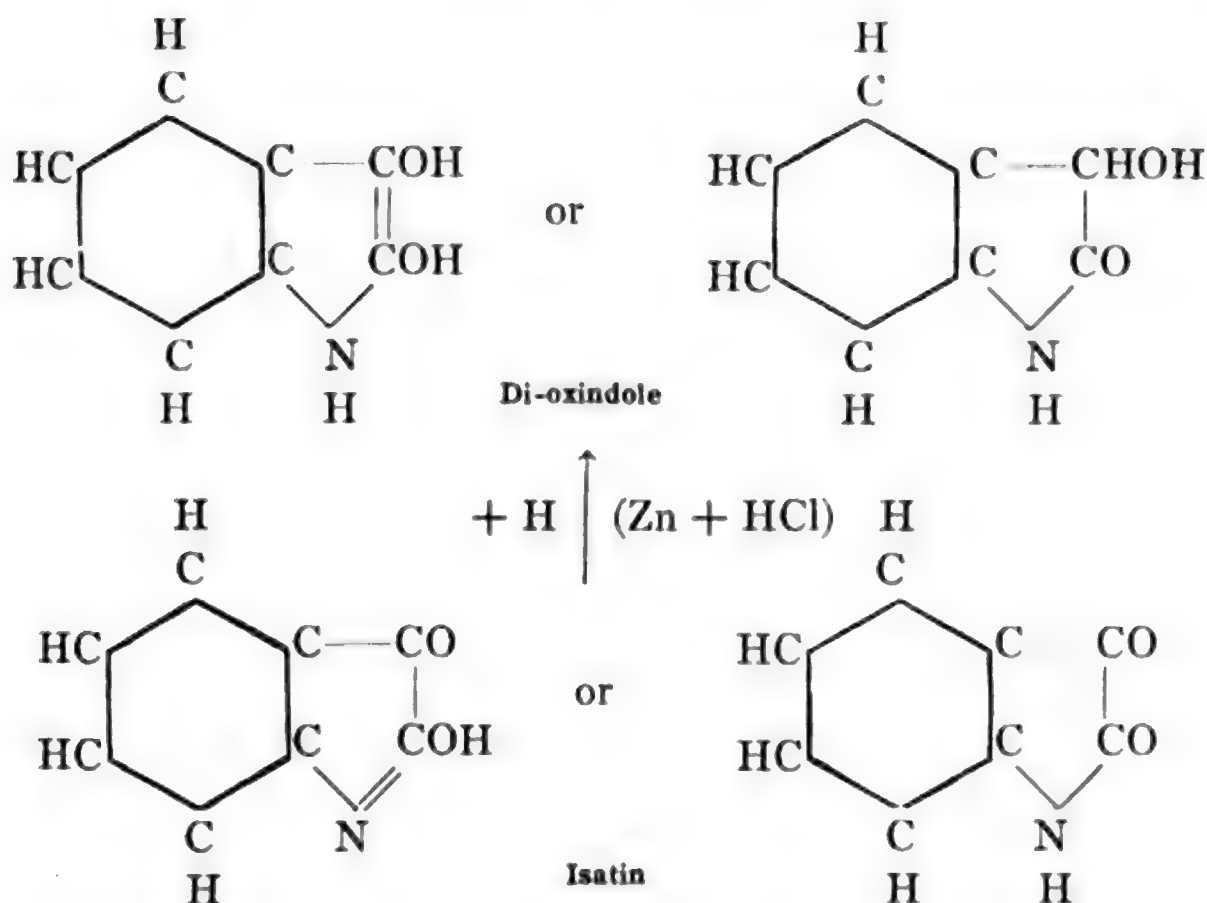
Di-oxindole yields oxindole by reduction with tin and hydrochloric acid.

Isatin.—Furthermore, a *di-ketone* derivative of di-hydro indole known as **isatin** is prepared from **ortho-amino benzoyl formic acid** as a lactam anhydride.

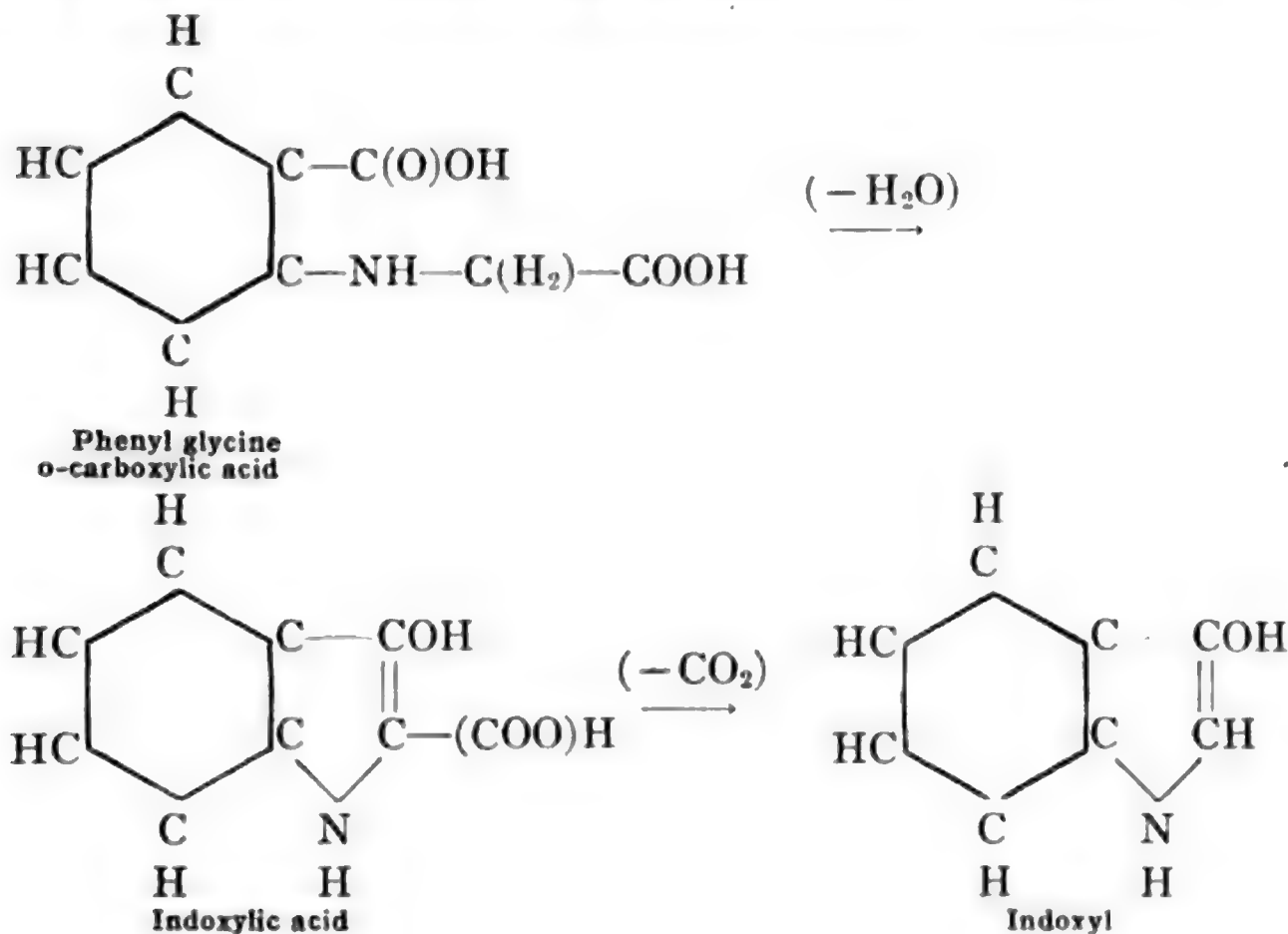


Isatin by reduction with zinc and hydrochloric acid yields di-oxindole. Putting these compounds together and showing their relationships as indicated by the syntheses just given, the constitution in each case is well established.





Indoxyl.—One more derivative of indole must be mentioned connected with the synthetic production of indigo. Isomeric with oxindole is another mono-hydroxy indole known as **indoxyl**. It is prepared from **phenyl glycine ortho-carboxylic acid**, **anthranil acetic acid**.

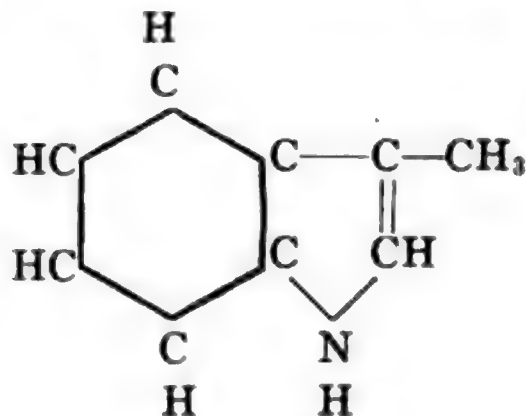


When phenyl glycine *ortho*-carboxylic acid is fused with potassium hydroxide it first loses water yielding an acid, **indoxyllic acid**, and this loses carbon dioxide yielding **indoxyl**. In indoxyl the hydroxyl group is in the 3-position while in the isomeric oxindole it is in the 2-position. All of these compounds are thus condensed hetero-cyclic compounds of a *benzene ring* and a *pyrrole ring*. Indole is the mother substance and the others are hydroxy or ketone derivatives.

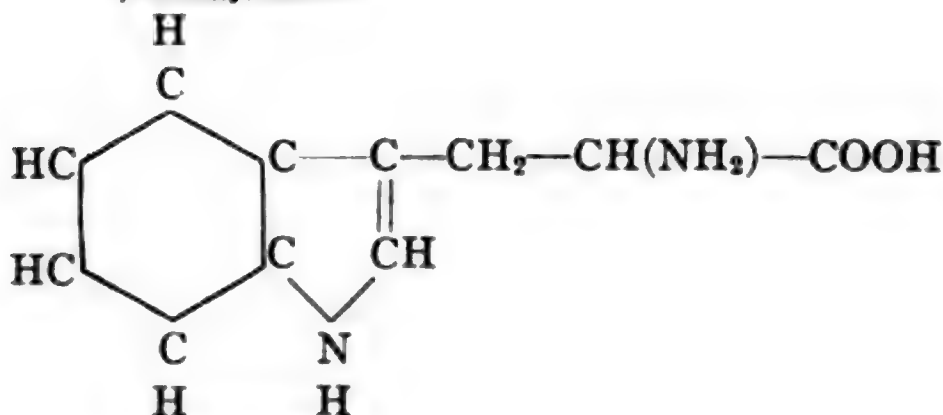
Skatole, Tryptophane

Skatole.—We have mentioned the fact that indole is important physiologically. Associated with indole in this relationship is the *beta*-methyl homologue of indole known as **skatole**. Skatole is the substance to which the characteristic odor of fæces is due. Both of these compounds are present in fæces and are the result of putrefactive decomposition of protein.

Tryptophane.—As an intermediate product in the decomposition of proteins we have the amino acid known as **tryptophane** which may be obtained by the acid hydrolysis of most proteins (p. 389). Tryptophane may be considered either as an indole or skatole derivative.

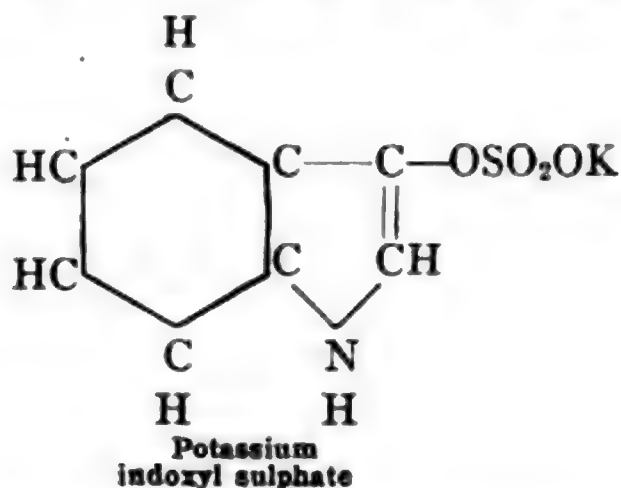


Skatole
 β -Methyl indole



Tryptophane
Skatole amino
acetic acid
 β -Indole α -amino propionic acid

On further decomposition tryptophane yields either indole or skatole. Not only are these final protein decomposition products present in the faeces, but they become absorbed from the intestine and pass into the urine where they are present as normal constituents, having first undergone oxidation forming indoxyl and skatoxyl which then esterify with sulphuric acid yielding, in the case of indole, **indoxyl sulphuric acid**, the potassium salt of which has been wrongly termed *indican*.



Skatol probably does not yield the corresponding sulphuric acid salt but is present in urine as the mono-carboxylic acid or as skatole cetic acid.

Indigo

What now is **indigo** and what is its relation to these compounds of the indole group? Indigo, which is sometimes called the *king of dyes*, is the most common and most valuable blue dye. It was originally obtained solely from the indigo plant and has been known for a long time. The chemical study of this natural dye, in order to determine its constitution and thus make possible its synthetic preparation, forms one of the most interesting and striking examples of the triumph of modern synthetic organic chemistry. Without attempting to discuss the subject in its historical development we shall show the final results of the study and its industrial application.

Aniline.—When **indigo** is distilled **aniline** is obtained, a fact which gave the name aniline to the product and which we referred to in discussing that compound (p. 539).

Anthranilic Acid.—Also from indigo we may obtain **anthranilic acid**

which is *ortho*-amino benzoic acid, C_6H_4

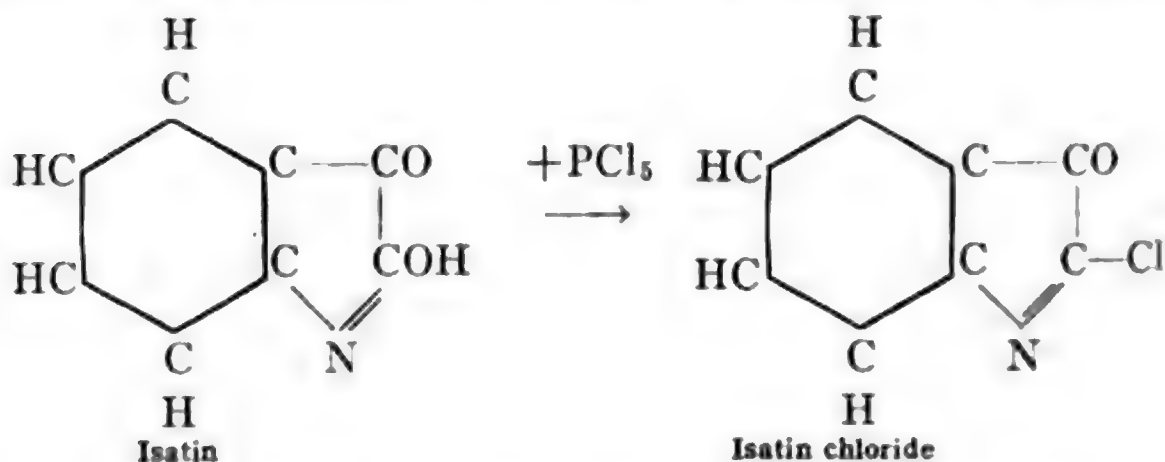
$$\begin{array}{l} \text{COOH (1)} \\ \text{NH}_2 \quad (2) \end{array}$$

Isatin, Indole, etc.—By oxidation indigo yields **isatin** which by successive reductions as recently explained yields **di-oxindole**, **oxindole** and finally **indole**. Also **indoxyl**, the isomer of oxindole, yields indigo by oxidation. The composition formulas of indigo and these last compounds are as follows:

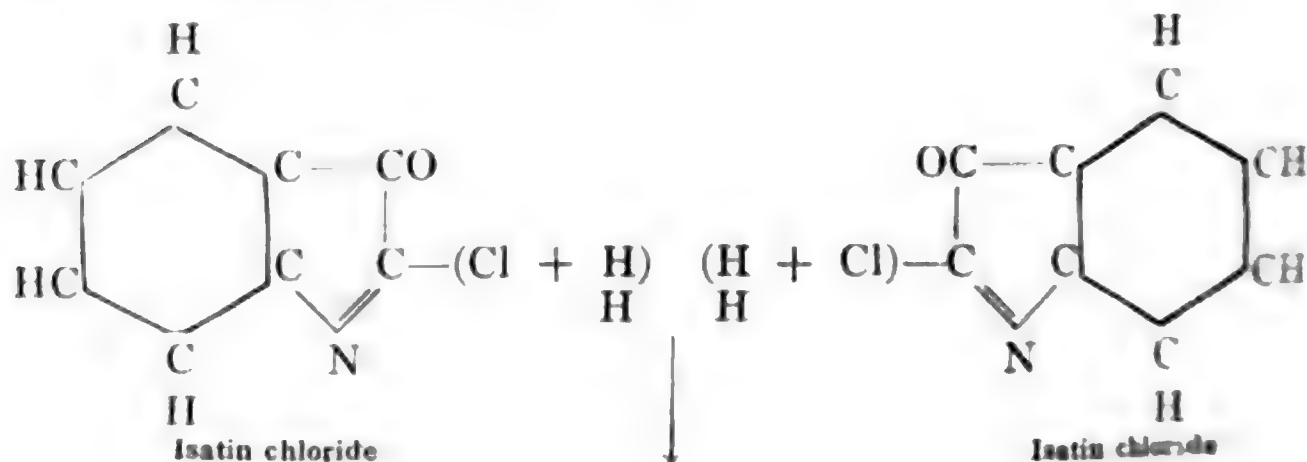
C_8H_7N	Indole
C_8H_7ON	Indoxyl and Oxindole
$C_8H_7O_2N$	Di-oxindole
$C_8H_5O_2N$	Isatin
$C_{16}H_{10}O_2N_2$	Indigo

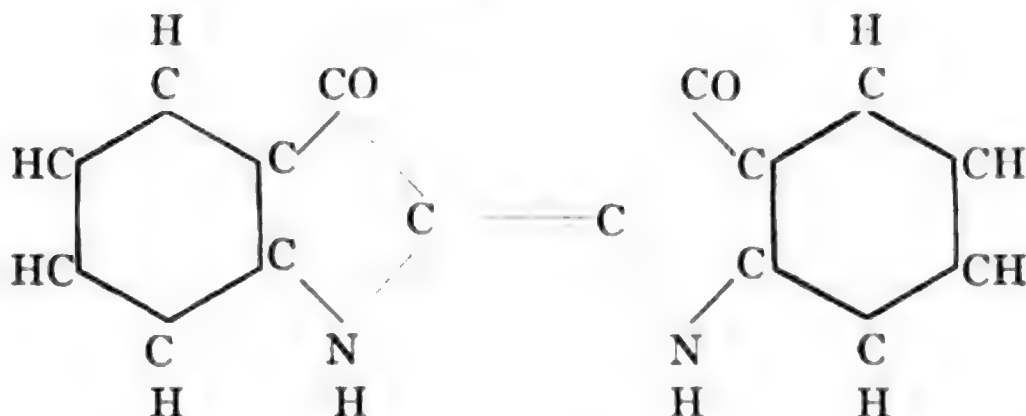
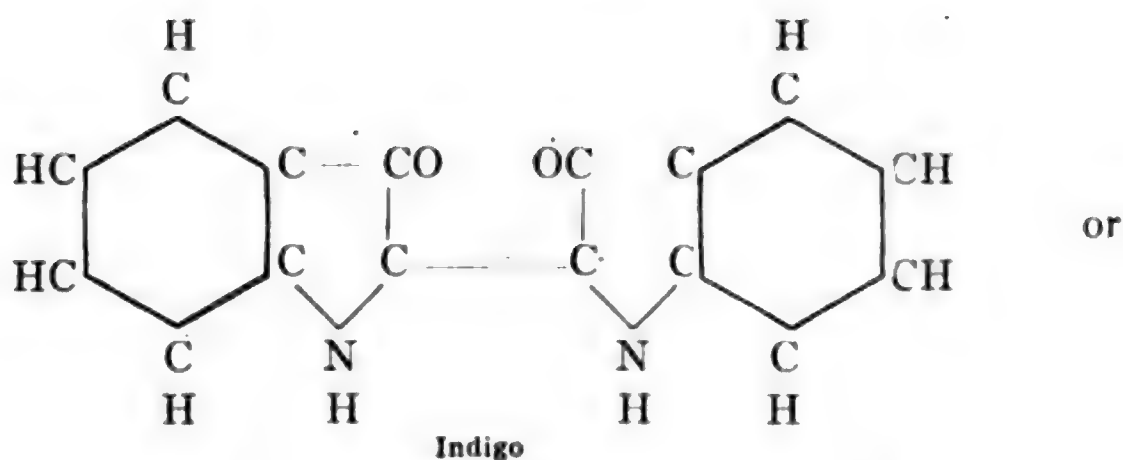
These facts alone indicate that indigo probably contains *two* indole groups or residues.

Isatin Chloride.—Now isatin which is a di-ketone of di-hydro indole, or the tautomeric form, a mixed ketone and hydroxyl derivative of indole, yields a chloride when treated with phosphorus pentachloride.



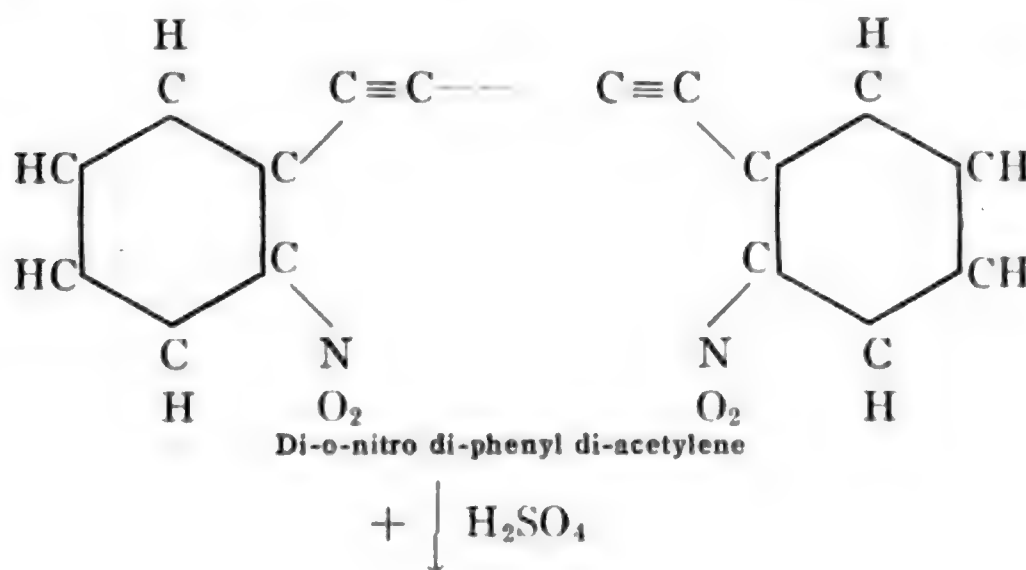
On treatment of isatin chloride with zinc dust and acetic acid the chlorine is eliminated and two hydrogens added with the formation of **indigo**. The reaction, with the formula for indigo which is supported, as we shall find, by other syntheses, is as follows:

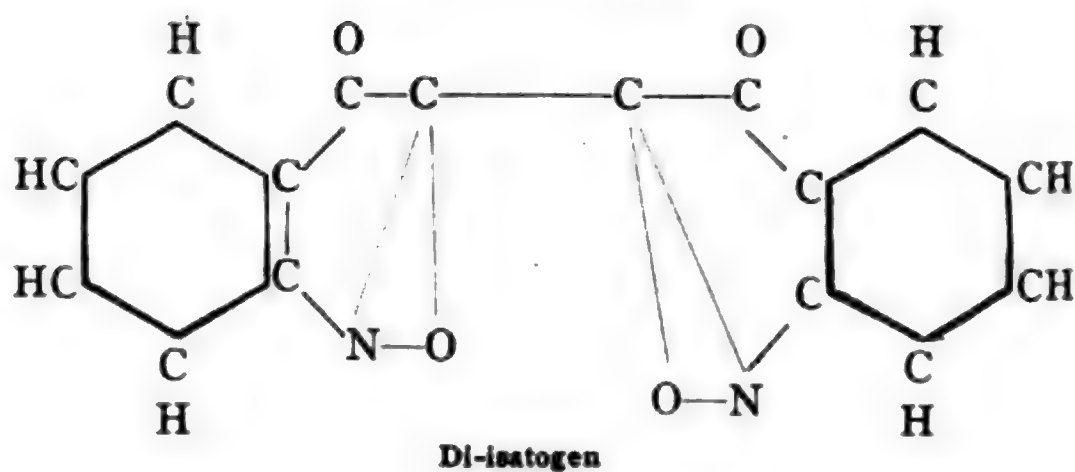




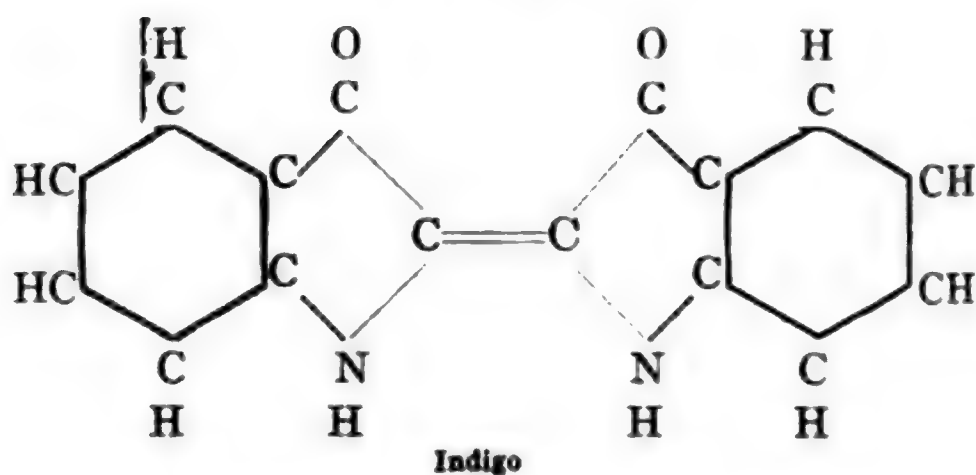
Synthesis.—There have been numerous syntheses of indigo some of which have been used industrially while others have been of importance in establishing the constitution of the dye.

From Di-phenyl Di-acetylene.—The proof that the two isatin or indole residues are *linked* together by *the carbons* is in the synthesis of indigo from **di-phenyl di-acetylene**, $C_6H_5-C \equiv C-C \equiv C-C_6H_5$. This compound by conversion into the di- (ortho-nitro) product, and treatment with sulphuric acid and reduction with ammonium sulphide, yields indigo. This indicates that the chain of carbon linkings remains as in the above compound.

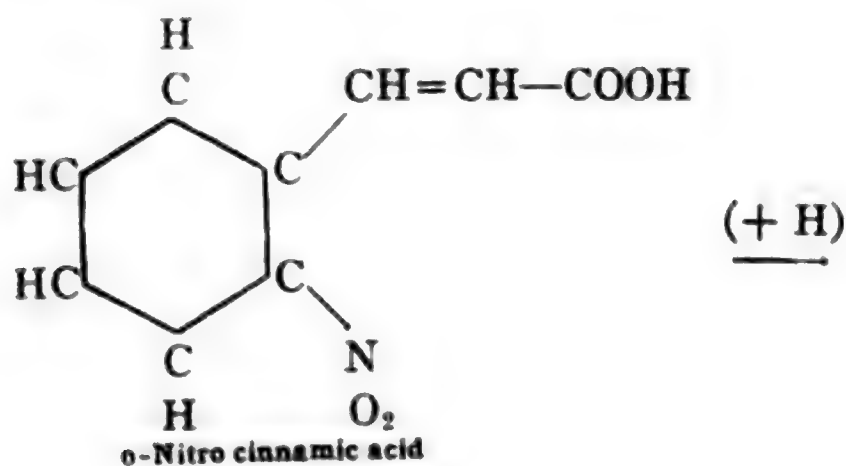


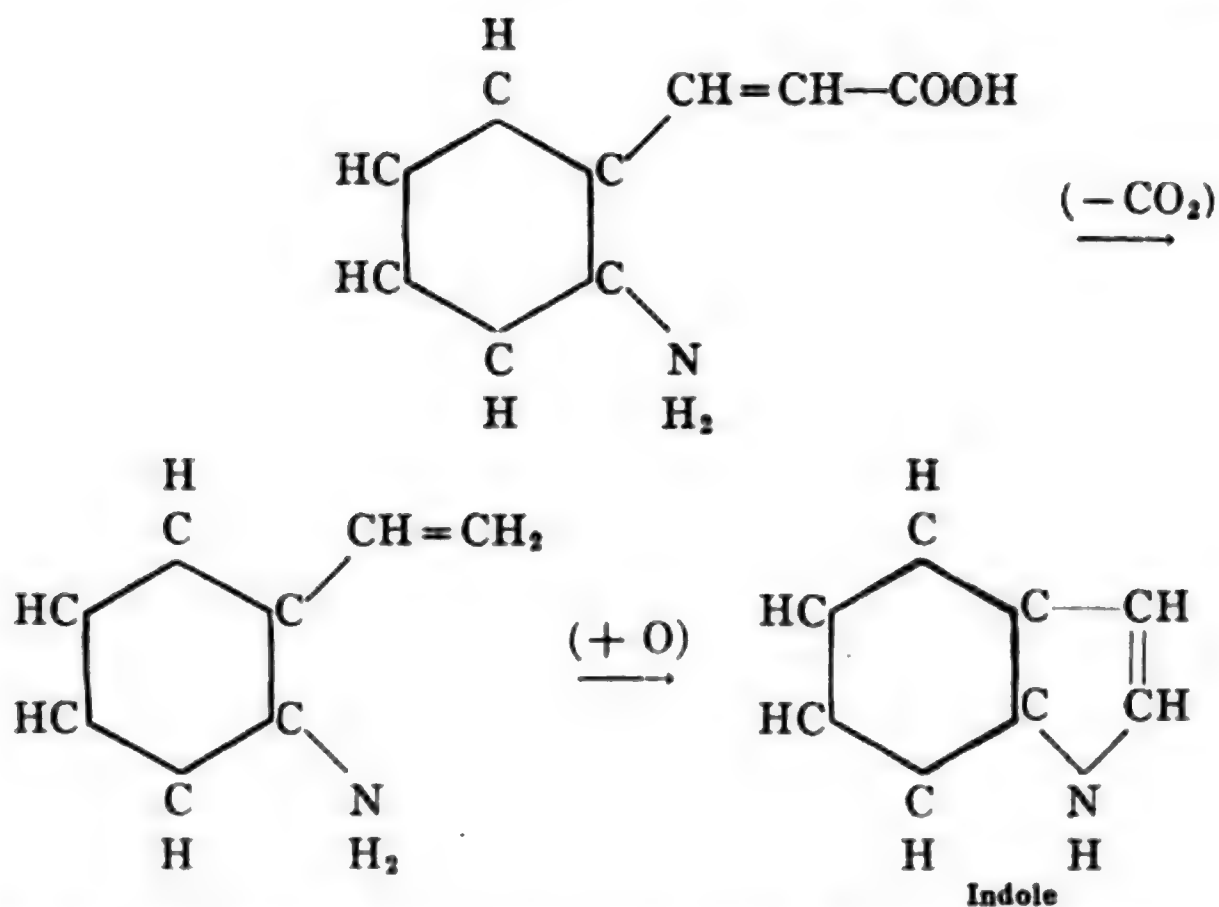


re | duction
↓



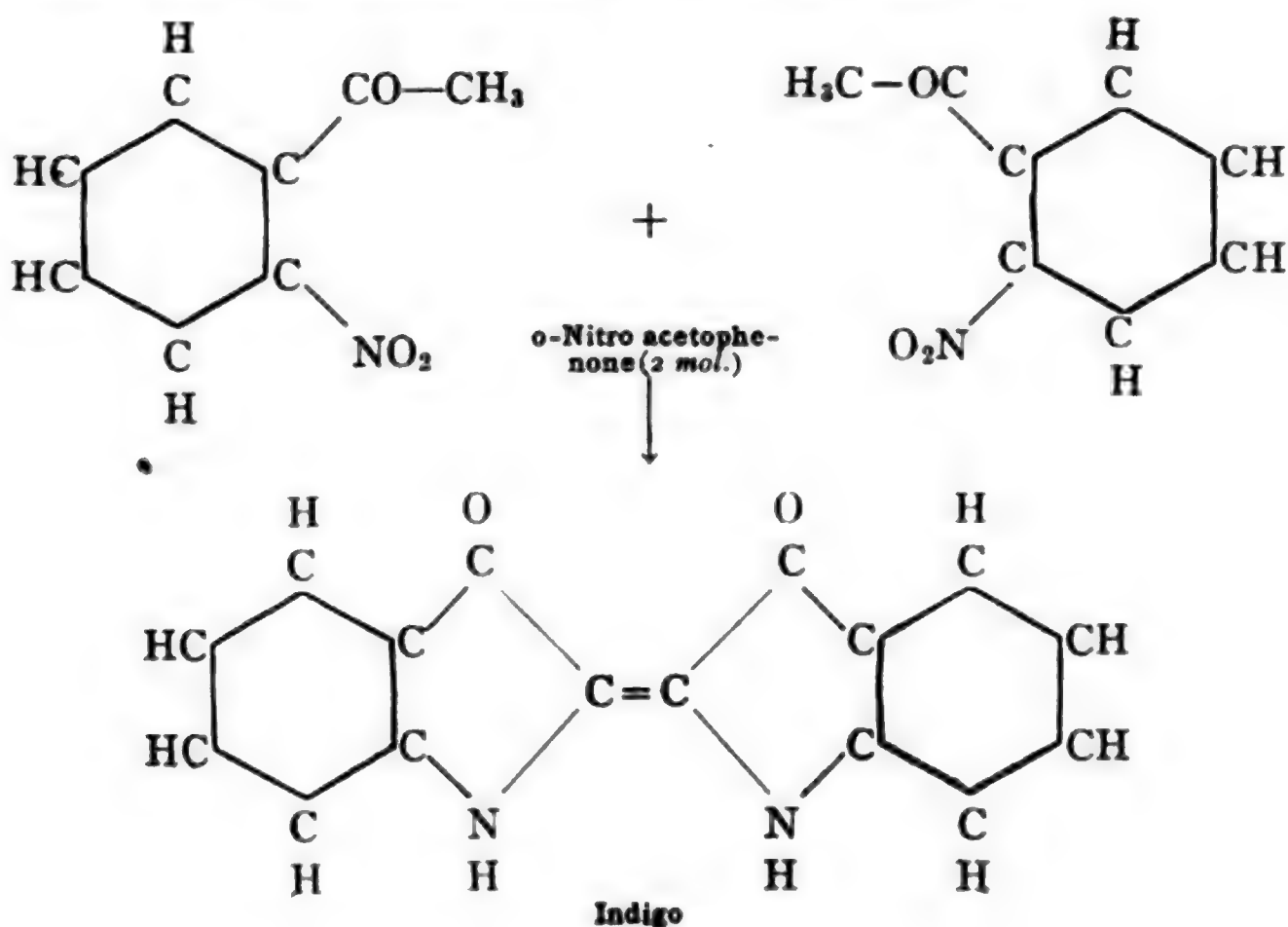
Baeyer and Emmerling, Indole from *ortho*-Nitro Cinnamic Acid.—The first relationship between members of the indole group and simpler benzene derivatives was that established by **Baeyer** and **Emmerling**, 1869, in synthesizing indole from *ortho*-nitro cinnamic acid by fusion with potassium hydroxide and iron filings. The steps in the synthesis are probably as follows:





Engler and Emmerling, Indigo from ortho-Nitro Acetophenone.—

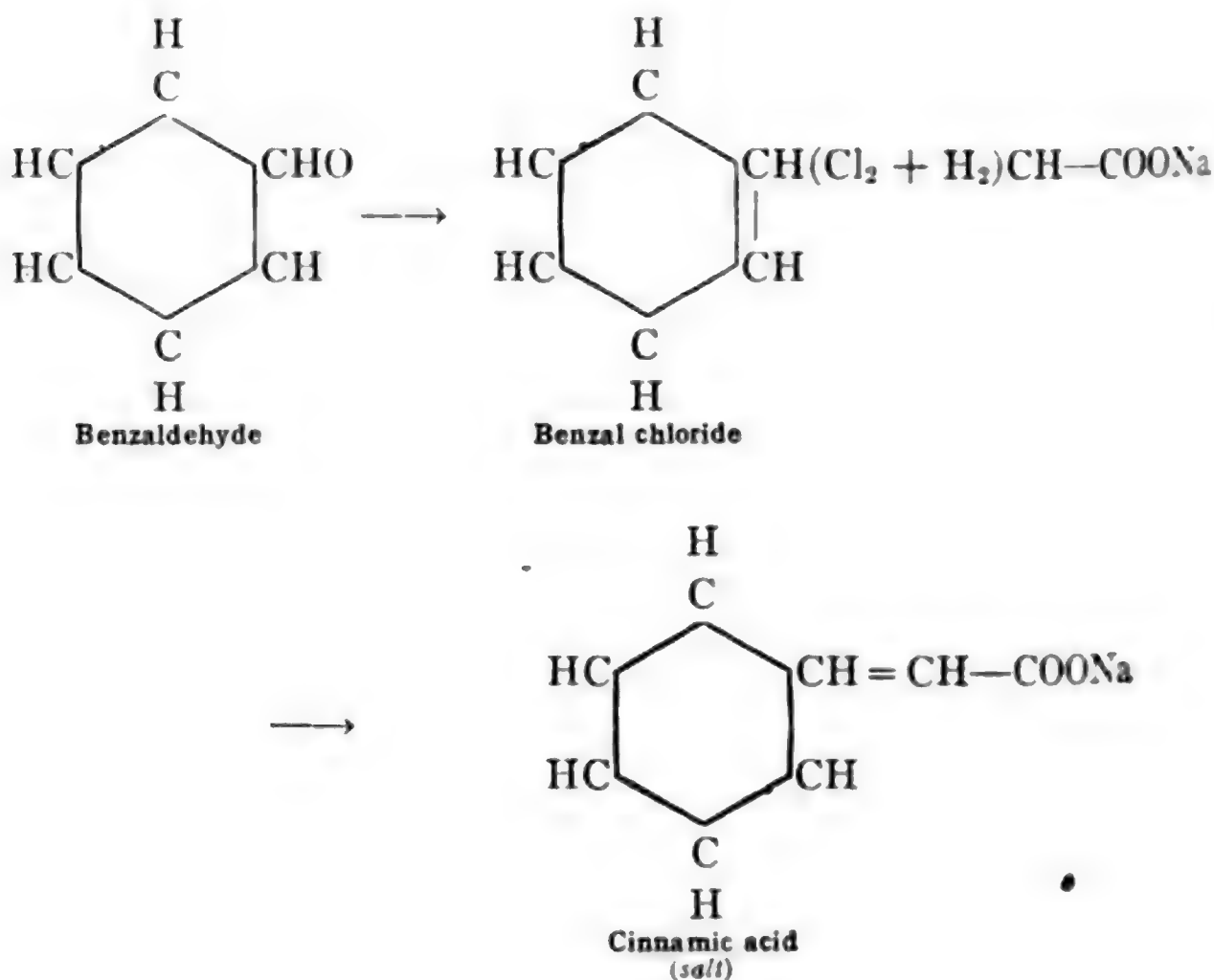
In 1870 **Engler and Emmerling** first synthesized indigo itself by heating **ortho-nitro acetophenone** with lime and zinc dust.



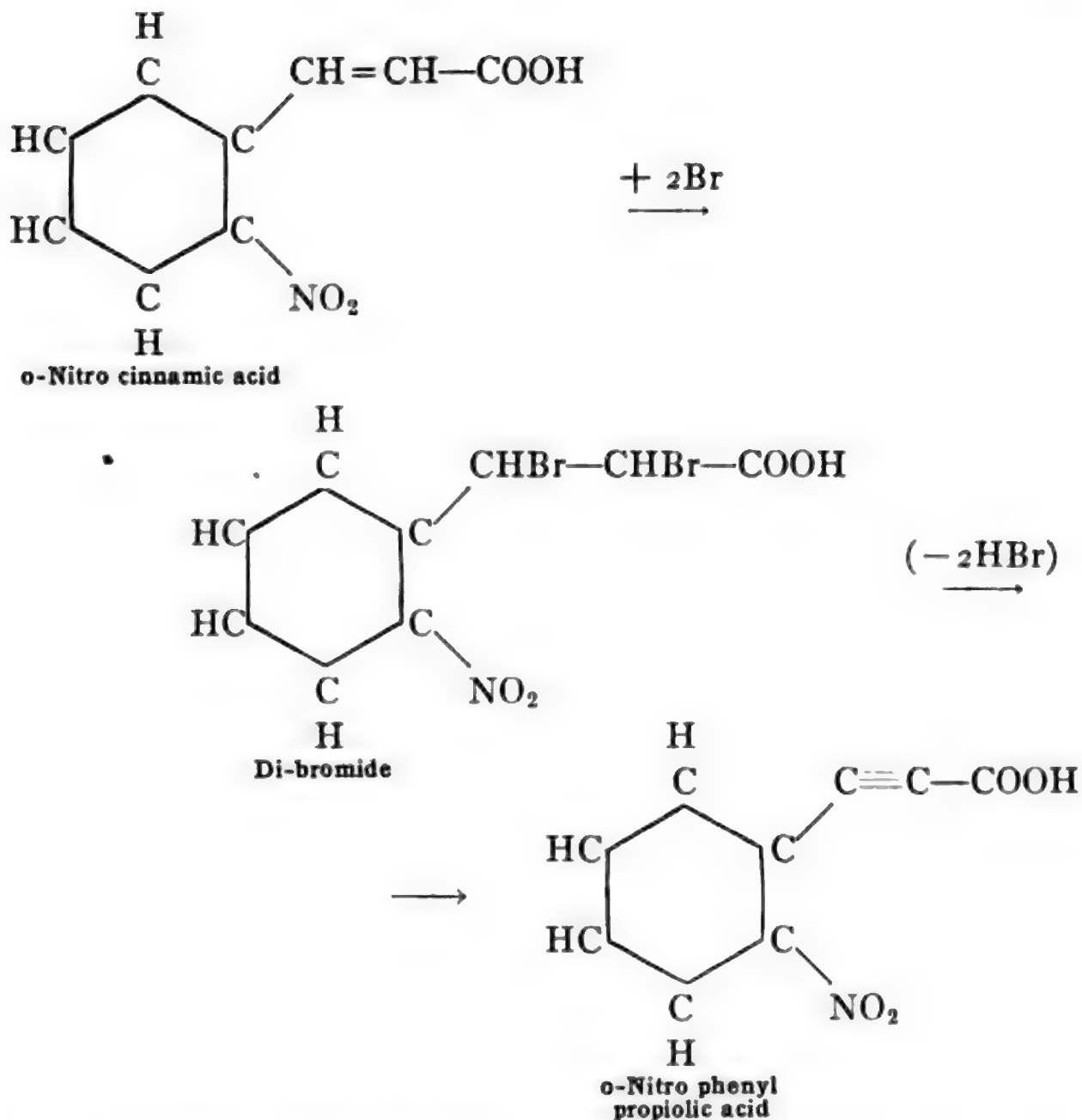
From **ortho-Nitro Phenyl Acetic Acid**.—Several other syntheses were developed by **Baeyer**. Starting with **ortho-nitro phenyl acetic acid**, $\text{C}_6\text{H}_4 \begin{matrix} \text{CH}_2\text{—COOH (1)} \\ \text{NO}_2 \end{matrix}$ (2), he obtained **oxindole** by the reaction

already given (p. 866). From oxindole by oxidation **isatin** was obtained and this through the chloride yielded **indigo** (p. 872).

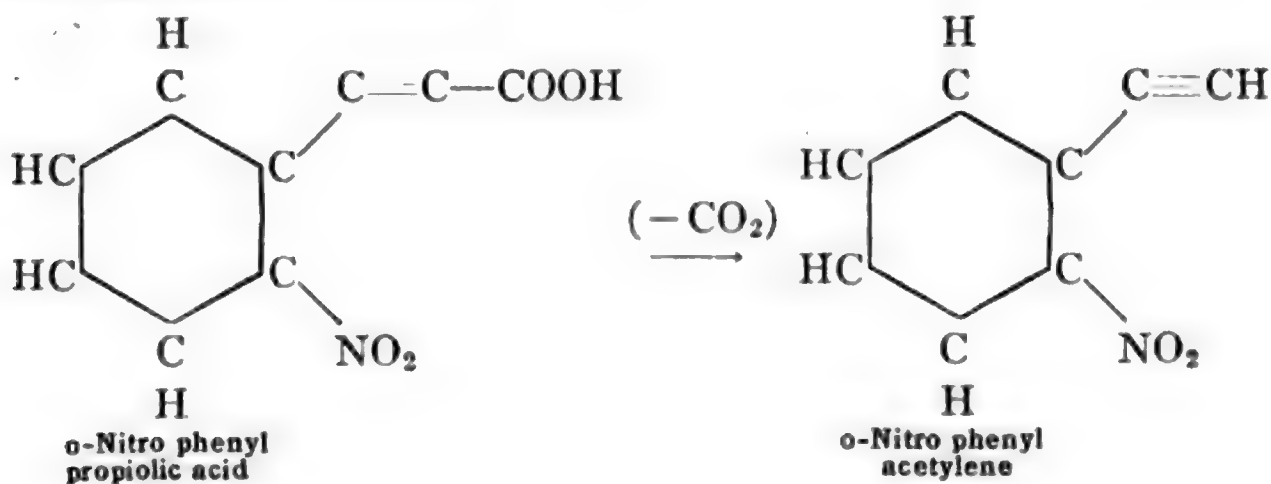
Benzaldehyde, ortho-Nitro Cinnamic Acid, ortho-Nitro Phenyl Propiolic Acid.—Later he started with **benzaldehyde** and obtained first **benzal chloride** which by condensation with sodium acetate yielded **cinnamic acid salt**.

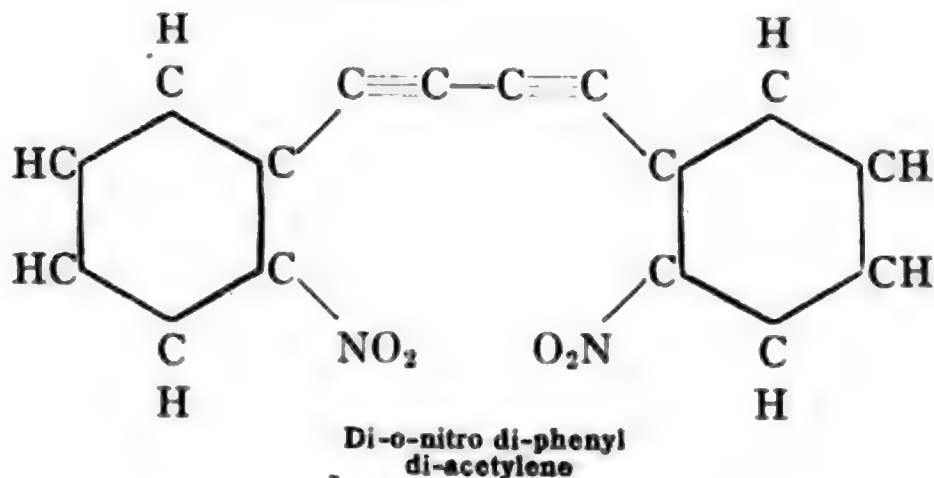
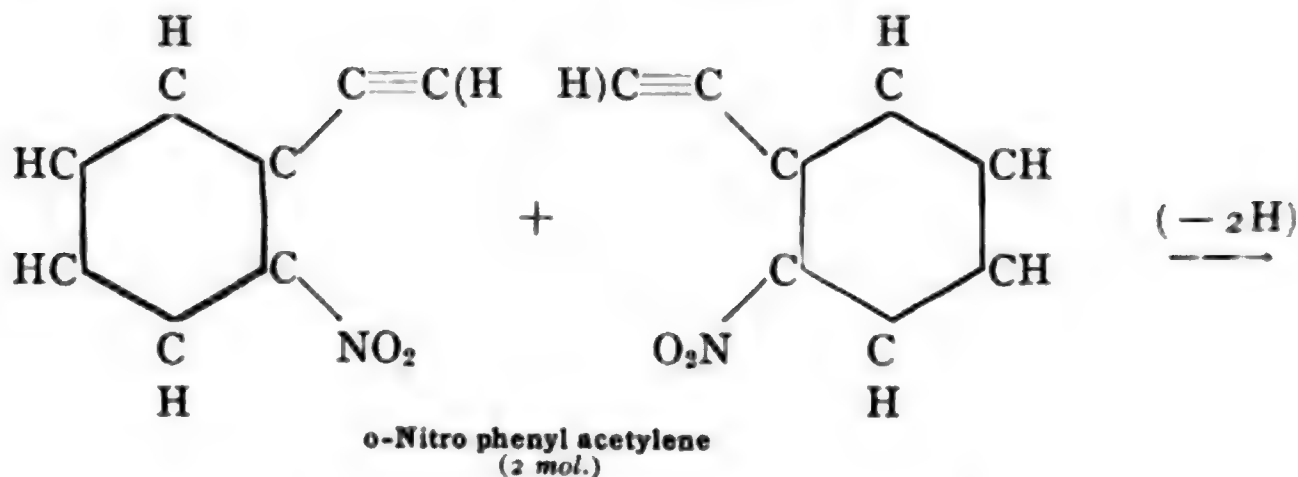


From the cinnamic acid salt by nitration he obtained **ortho-nitro cinnamic acid**. This yielded a *di-bromide* which by loss of two molecules of hydrogen bromide was converted into **ortho-nitro phenyl propiolic acid** (p. 700).

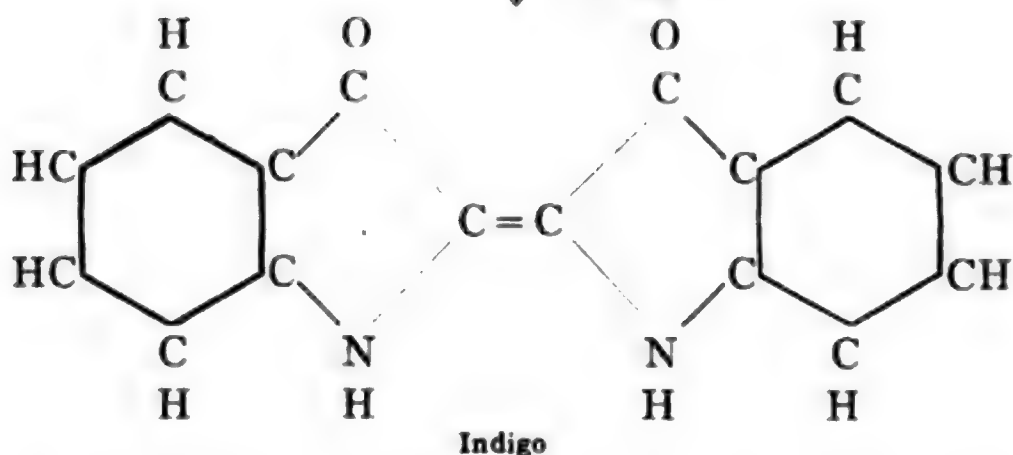


Finally **ortho-nitro phenyl propiolic acid** when heated with alkali and glucose, the latter acting as a reducing agent, yielded **indigo**. He also converted *ortho*-nitro phenyl propiolic acid into indigo by the following series of reactions.



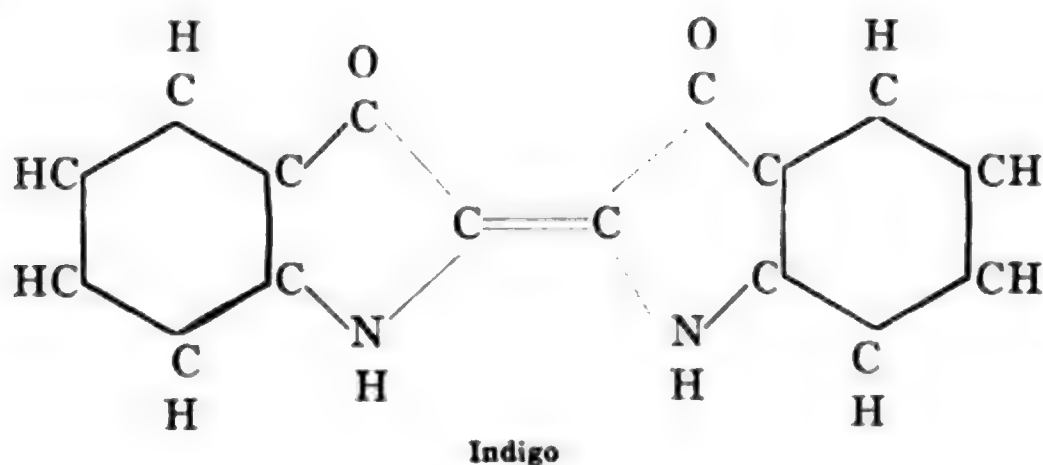
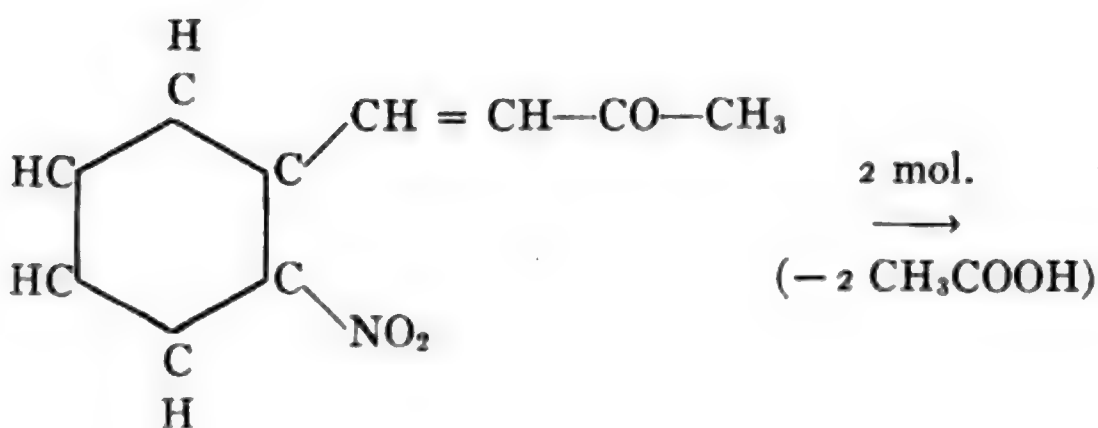
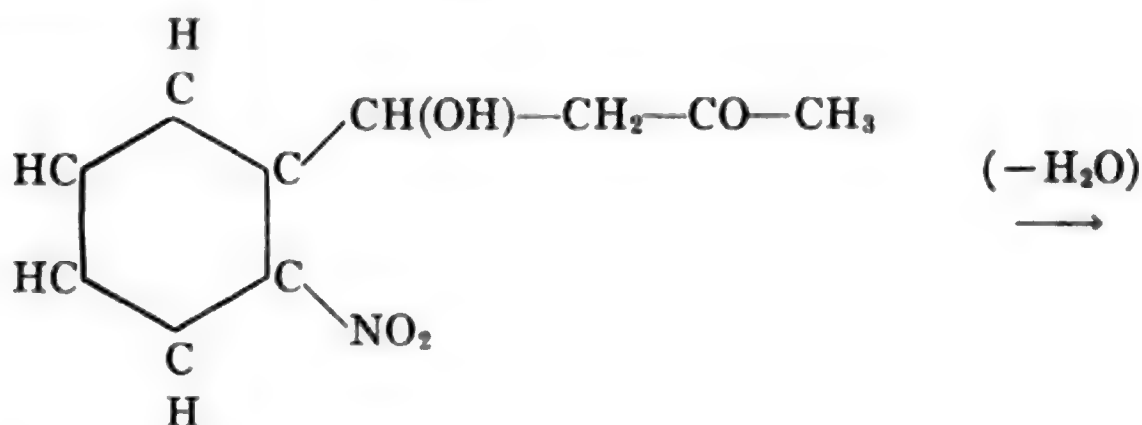
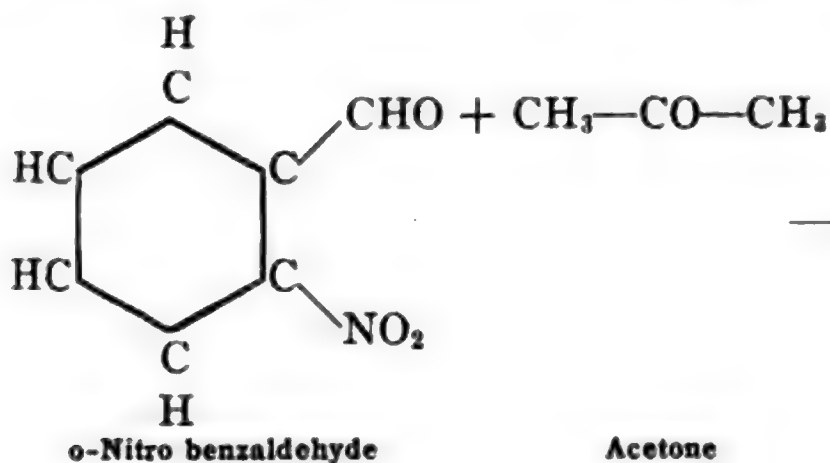


re-arrangement
to di-isatogen
and reduction
(p. 873)



The reaction probably proceeds as above, by the loss of carbon dioxide with the formation of **ortho-nitro phenyl acetylene**. This condenses with itself by the loss of two hydrogens yielding **di-ortho-nitro di-phenyl di-acetylene** and this, by the reactions previously discussed (p. 874), rearranges to **di-isatogen** which by reduction yields **indigo**. This synthesis, though at first used on an industrial scale, was not however a commercial success as the yield of ortho-nitro cinnamic acid was too small and the loss in the final stage was too large.

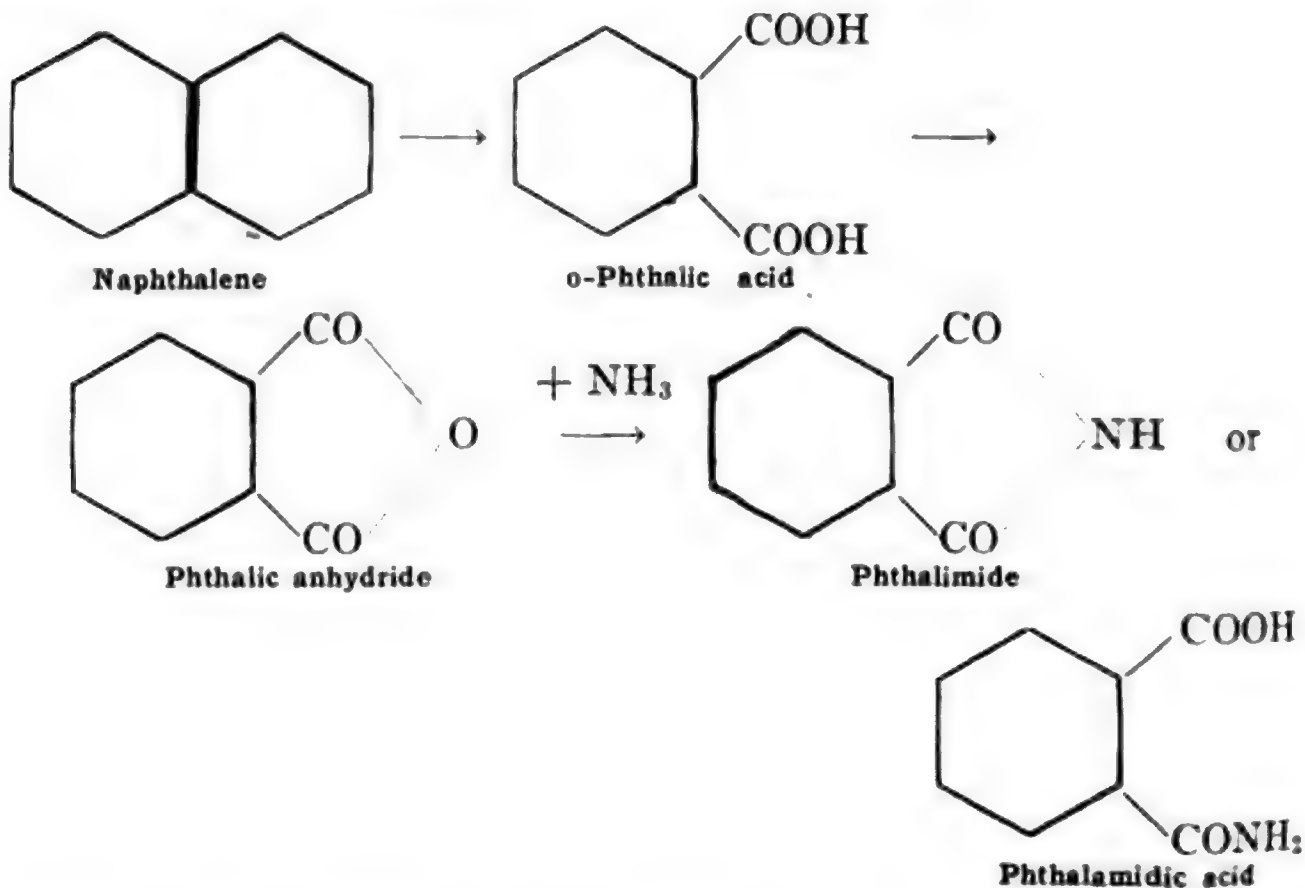
Baeyer and Drewsen, ortho-Nitro Benzaldehyde.—A later synthesis of **Baeyer and Drewsen** was by the condensation of *ortho*-nitro benzaldehyde with acetone in the presence of sodium hydroxide.



The commercial value of this synthesis was increased when it was found that benzaldehyde could be prepared directly from **toluene**. Like the preceding synthesis of **Baeyer**, however, it has proved too expensive for a general industrial process though it is still used in some cases.

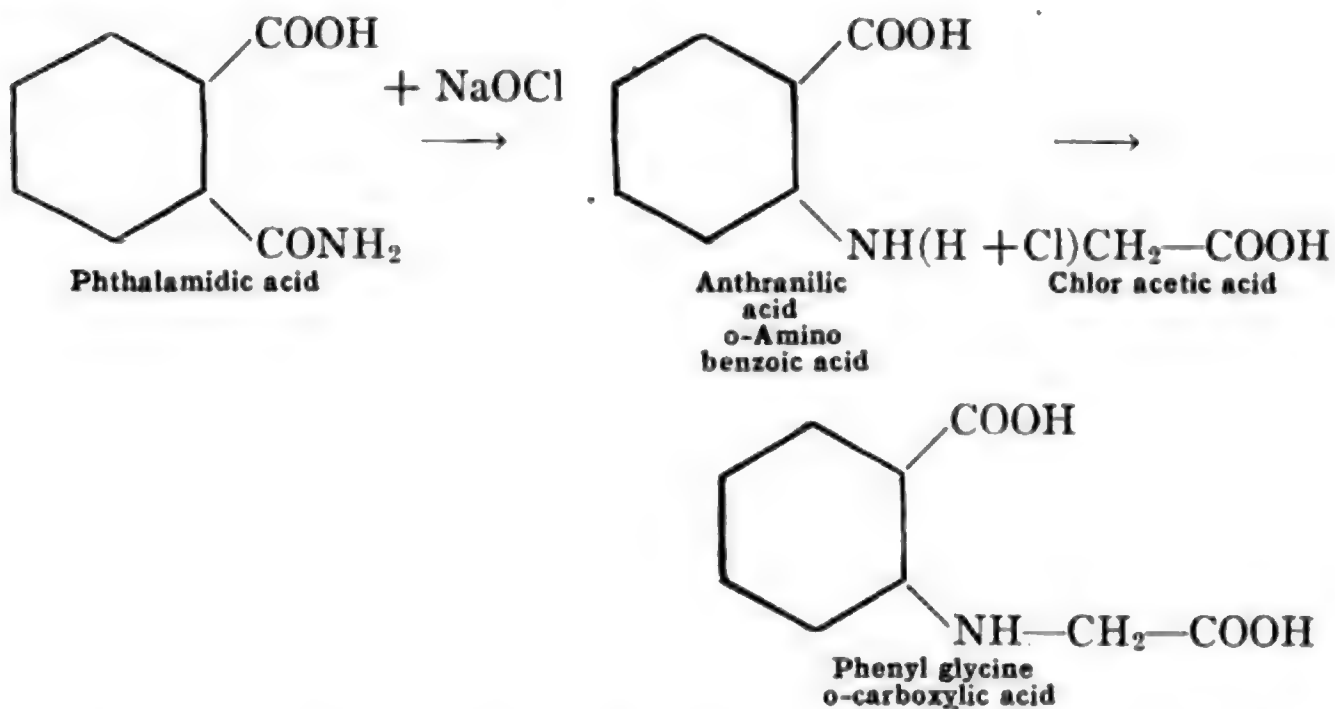
Heumann's Synthesis, Phenyl Glycine Ortho-carboxylic Acid.—The synthesis that has resulted in placing synthetic indigo on the market is that of **Heumann** by the fusion of **phenyl glycine ortho-carboxylic acid** with caustic potash. The product of this fusion is **indoxyl** which by atmospheric oxygen is oxidized to **indigo**. The industrial success of this synthesis was achieved only when the preparation of the phenyl glycine ortho-carboxylic acid from a cheap source was accomplished.

Naphthalene to Anthranilic Acid.—Such a cheap source was found in **naphthalene** which was converted into **anthranilic acid**, **ortho-amino benzoic acid**, and this by treatment with **chlor acetic acid** yields **phenyl glycine ortho-carboxylic acid**. The complete synthesis is as follows: **Naphthalene** is oxidized to **ortho-phthalic acid** which then yields **phthalic anhydride**. This with ammonia, as ammonium carbonate, yields **phthalimide** or **phthalamidic acid**.

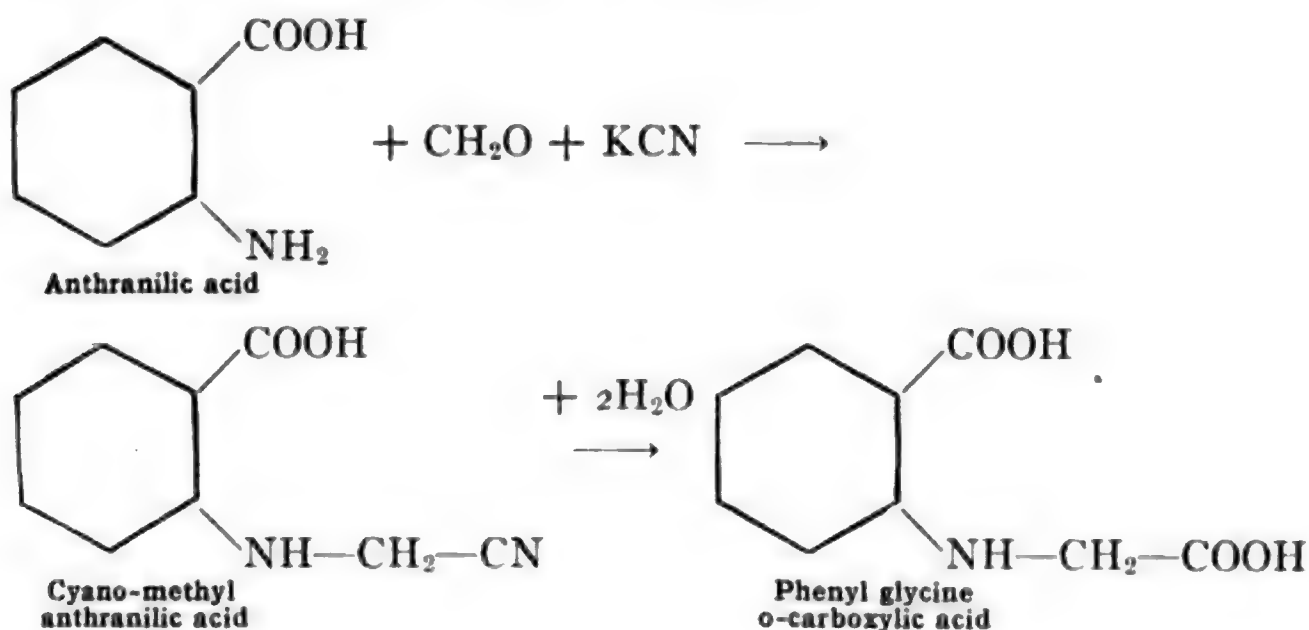


Phthalamidic acid is then converted into **anthranilic acid** by the action

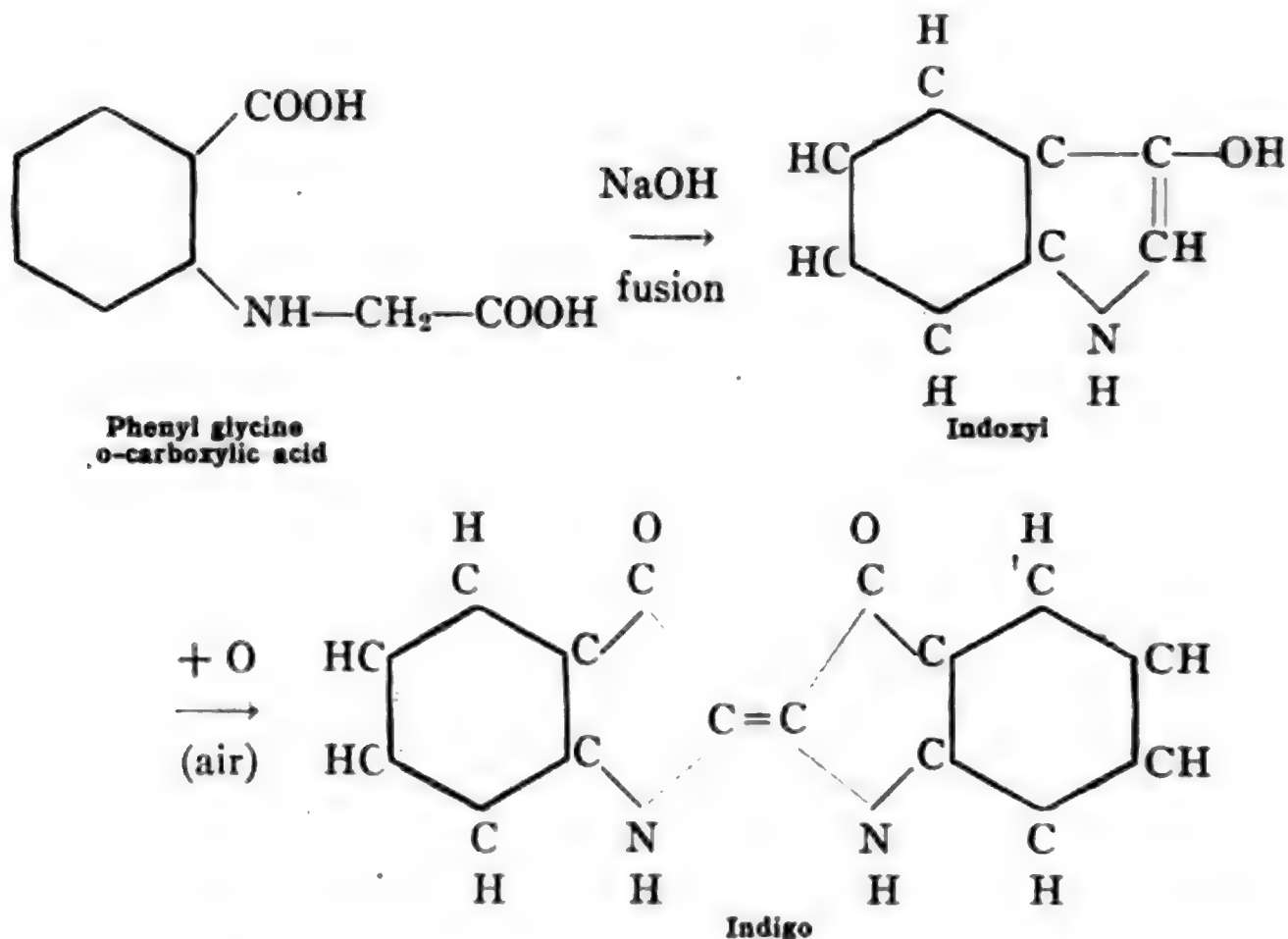
of sodium hypochlorite or hypobromite as in the **Hofmann** reaction (p. 148), and the anthranilic acid with chlor acetic acid yields **phenyl glycine *ortho*-carboxylic acid**.



The anthranilic acid may also be converted into phenyl glycine *ortho*-carboxylic acid by the action of formaldehyde and potassium cyanide, yielding first **cyano-methyl anthranilic acid** which on hydrolysis is converted into the phenyl glycine compound.



Finally the **phenyl glycine *ortho*-carboxylic acid** is fused with sodium hydroxide and converted into **indoxyl** which by atmospheric oxidation yields **indigo**.



In the reactions above the products are given in the form of the free acids though in fact the sodium or potassium salts are usually obtained. In practice the free acid may be secured by acidifying though the salts are often used.

Industrial Indigo.—These syntheses of indigo have been considered rather thoroughly because, as previously mentioned, the whole problem of the industrial synthesis of this natural dye is one of the triumphs of synthetic organic chemistry and it illustrates in a striking way how complete must be the study of such a problem in order that success may result. It also shows how the study of the constitution of a compound must be supplemented by a search for a particular synthesis involving a cheap commercial material as the starting point. The magnitude of the task may be grasped by the consideration of a few facts. The period of time from the first synthesis of indole and indigo to that of the full establishment of the constitution of indigo was about ten years. From the first apparently commercial synthesis of indigo by **Baeyer**, until **Heumann's** better synthesis, another ten years elapsed; and the improvement of **Heumann's** process, with the finding of a cheap starting point and the commercial struggle to make the process an

industrial success, occupied about twenty years more. Thus from 1869 until 1909 the problem of synthetic indigo occupied the attention of some of the world's greatest organic chemists and required the expenditure of large sums of money in purchasing patents and erecting manufacturing plants. The first patents of **Baeyer** were sold for some one hundred thousand dollars and probably as much was paid for those of **Heumann**. The first plant for the production of synthetic indigo cost over two million dollars and the capitalization of the combined synthetic indigo companies of Germany amounts to about five million dollars.

In 1907 the total production of synthetic indigo was about 80 per cent of the world's consumption. The price of the synthetic compound was about \$1.50 a pound and the natural about \$1.75.

The increase in the production of the synthetic indigo has decreased the cultivation of the indigo plant, especially in India where the land formerly used for this purpose is now used for other crops such as rubber, turmeric, hemp, cotton, etc.

Natural Indigo.—Indigo is obtained naturally from the indigo plant, *Indigofera tinctoria*, which is cultivated in tropical countries, e.g., India, Java, and China. It is one of the oldest and most valuable dyes having been used in Egypt as early as 1600 B. C. and is still used more universally than any other blue dye. It occurs in the plant in the form of a glucoside known as **indican**. When the plants are extracted with warm water a natural ferment present in the plant hydrolyzes the glucoside into its constituent parts, viz., glucose and the leuco base of the dye or **indigo white**. After the extraction and fermentation the extract is aerated when the leuco base is oxidized and indigo results. It is a dark blue substance easily powdered and giving a coppery luster when rubbed. It sublimes at 170° to a red vapor. It is insoluble in water, alcohol, ether, acid or alkali, dissolving slightly in hot amyl alcohol, chloroform, carbon di-sulphide, etc. Concentrated sulphuric acid forms a mono-sulphonic acid which is soluble in water but insoluble in salt solution. Fuming sulphuric acid forms a di-sulphonic acid known as **indigo carmine**. Technically indigo is classed as a *vat dye*. It dyes both animal and vegetable fibers without a mordant. An explanation of the name *vat dyes* will be found in special books on dyes.

D. ALKALOIDS

The group of compounds known as **alkaloids** includes substances usually characterized by marked physiological activity. They occur most commonly in plants though some are found in animals. In their chemical character they are complex organic nitrogen bases generally insoluble in water but yielding salts which are usually soluble. Some authors classify as alkaloids all organic nitrogen bases which occur in plants. The basic character of the compounds is indicated in their names by the termination *ine*. While it is difficult to define or classify the alkaloids with exactness the characters just given may be considered as the essential ones. The best idea of the group may be gained by considering a brief list of those which we shall discuss. They are as follows: **conine, piperine, nicotine, quinine, cinchonine, strychnine, brucine, morphine, codeine, hyoscyamine, atropine, tropine, cocaine, stovaine, novocaine, caffeine, theobromine, xanthine, guanine and adenine.**

In this list there will be recognized, at once, several substances which have long been known and used in medicine because of their physiological and therapeutic properties. Several of them, also, are generally considered as deadly poisons because, in overdoses, the effect upon human beings is fatal. The physiological action on the animal body is of different types. In some cases partial or complete insensibility of the nervous system is produced. Those which act in this way include the *narcotics* such as **morphine**. In other cases a stimulation of the nerves or of the heart results as with **atropine, strychnine**, etc. Some act in a milder way and cause a lowering of the body temperature. These include the *anti-pyretics* or *febrifuges* such as **quinine**.

The reason for considering these compounds in this the last chapter of the book is not because they are more complex or less known than some other groups but because in their chemical classification most of those we shall study are related to the two hetero-cyclic compounds recently discussed, viz., **pyridine** and **quinoline**.

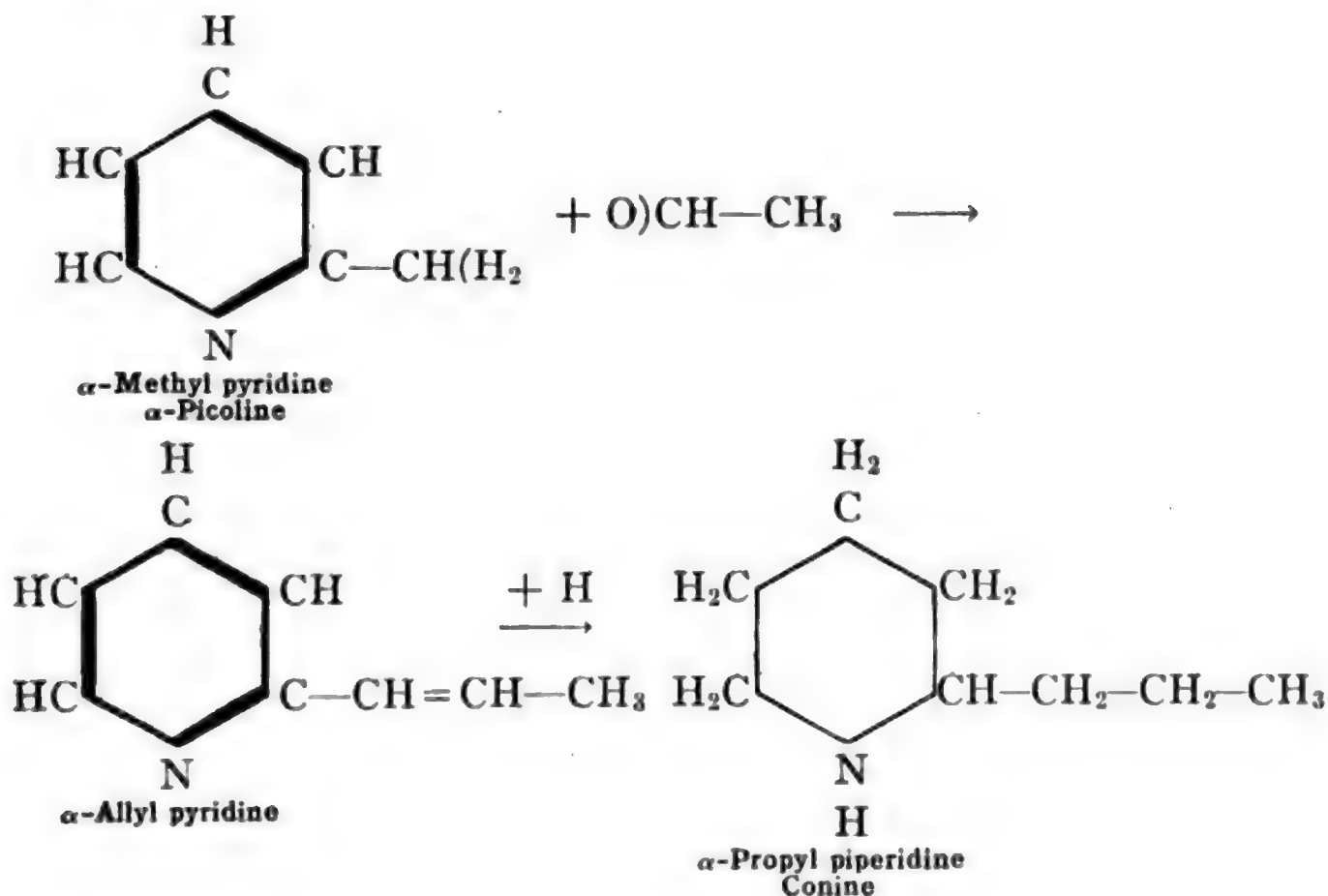
It should be stated that the treatment which follows is in no sense exhaustive either as to the properties, etc., of the alkaloids referred to, or as to the methods and reactions by which the constitution, when known, has been established. All that is attempted here is a brief presentation of the more common and important members, their origin and properties and their constitution as related to compounds we have previously studied.

ALKALOIDS RELATED TO PYRIDINE

Conine

The first alkaloid which we shall consider is of especial interest historically. The Greek philosopher **Socrates** was put to death by being compelled to drink an extract of hemlock, *Conium maculatum*. In the fruit and leaves of this plant there are present six different alkaloids one of which is named from the plant and is known as **conine**. This compound is a colorless, strongly alkaline liquid acting as a deadly poison when taken in more than extremely small doses. Physiologically it produces paralysis of the motor nerve terminations and depression of the central nervous system.

Conine is also of especial interest because it is the first natural alkaloid to have been made synthetically. In 1886 Ladenburg prepared it from *alpha*-picoline which is *alpha*-methyl pyridine. By condensing this with acetaldehyde he obtained *alpha*-allyl pyridine and by reduction this yielded the corresponding saturated compound, viz., *alpha*-propyl piperidine. This proved to be *inactive conine* and from it the dextro and levo isomers were obtained. The dextro conine thus prepared is identical with the natural alkaloid of hemlock. The reactions are as follows:

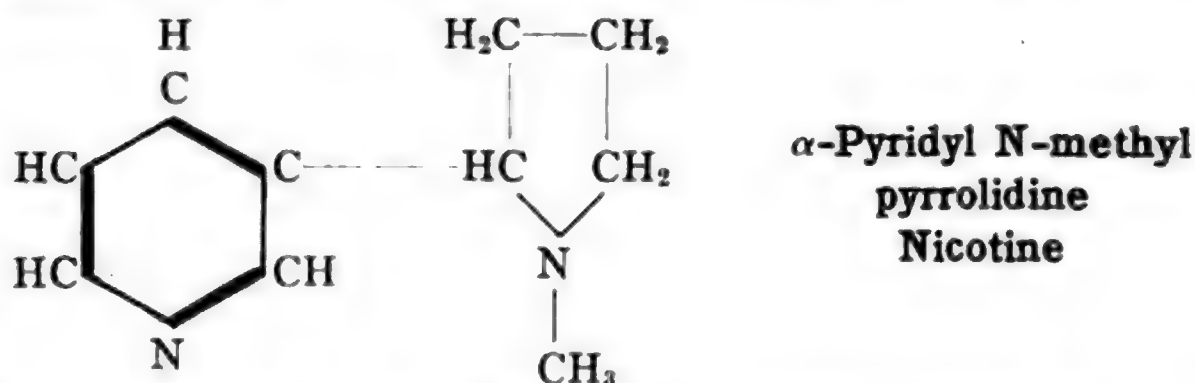


Piperine

The fruit of the plant *Piper nigrum* is the common black pepper of the household. This fruit yields an alkaloid known as **piperine** present to about 4 to 9 per cent in commercial pepper. On hydrolysis the alkaloid yields **piperidine** or hexa-hydro pyridine and an acid known as **piperic acid**. Piperine is thus considered as a piperidine amide of piperic acid. Physiologically this alkaloid acts like quinine but is less active and is uncertain. It is only rarely used in medicine.

Nicotine

The alkaloid **nicotine** is present in tobacco, *Nicotiana tabacum*. In discussing the derivatives of pyridine it was stated (p. 858) that the *beta*-mono-carboxy acid of pyridine is known as **nicotinic acid** and that it is obtained by the oxidation of the alkaloid nicotine. Therefore the alkaloid undoubtedly contains the pyridine group. It has been synthesized by **Pictet** and its constitution established as a **pyridine** derivative of **methyl pyrrolidine**. This constitution was first suggested by **Pinner**.



Natural nicotine is the levo variety. Physiologically the alkaloid affects both the central and peripheral nerves and increases the activity of the secreting glands. In more than minimum doses it is a poison. It is not used to any extent in medicine though recently it has been suggested as a hypodermic in cases of tetanus. The salicylic acid salt is also used somewhat for skin diseases. Tobacco extracts and also powdered tobacco are used as insecticides, their value depending upon the amount of nicotine present.

ALKALOIDS RELATED TO QUINOLINE

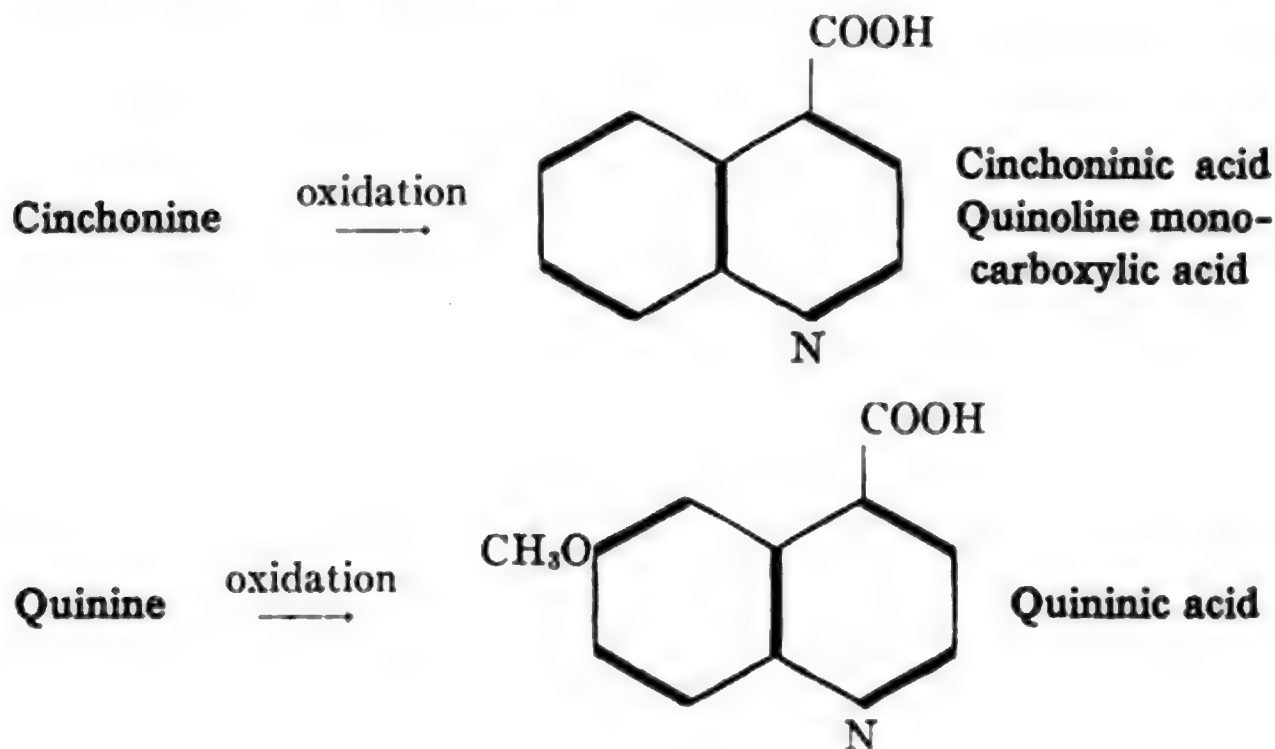
The alkaloids related to quinoline include three which are frequently used in medicine and on that account are commonly known. These

three are the almost universal *febrifuge*, **quinine**, the *stimulant* or *tonic*, **strychnine** and the *narcotic*, **morphine**. The first two are related to **quinoline** and the last to **iso-quinoline**.

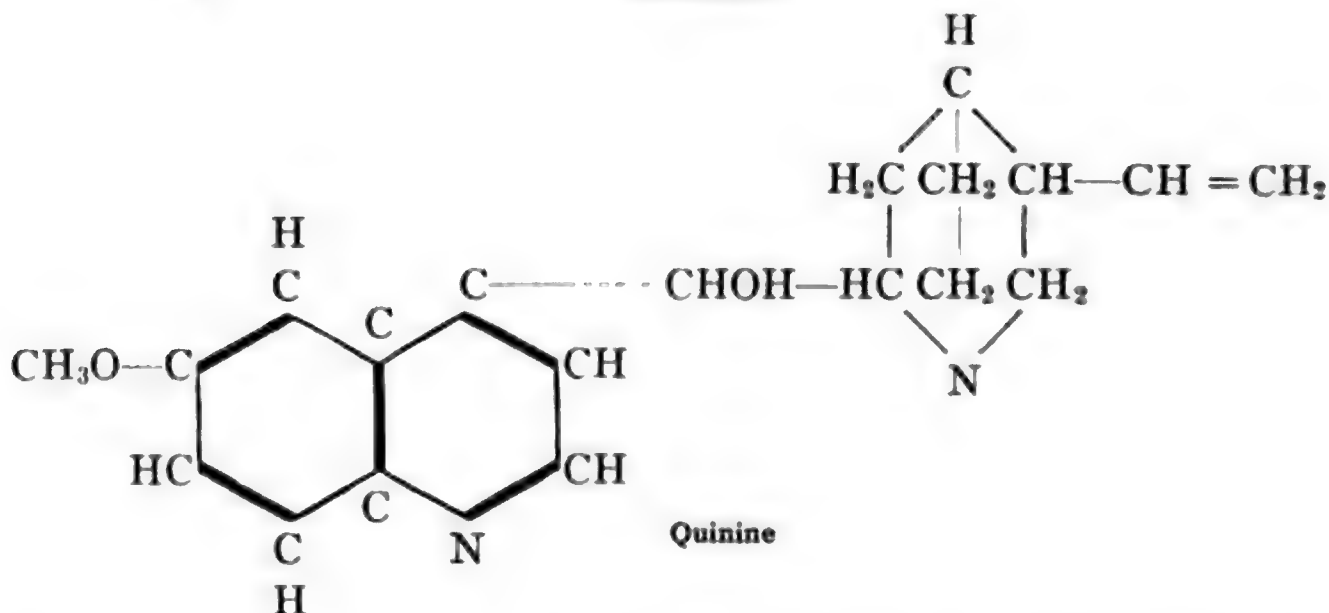
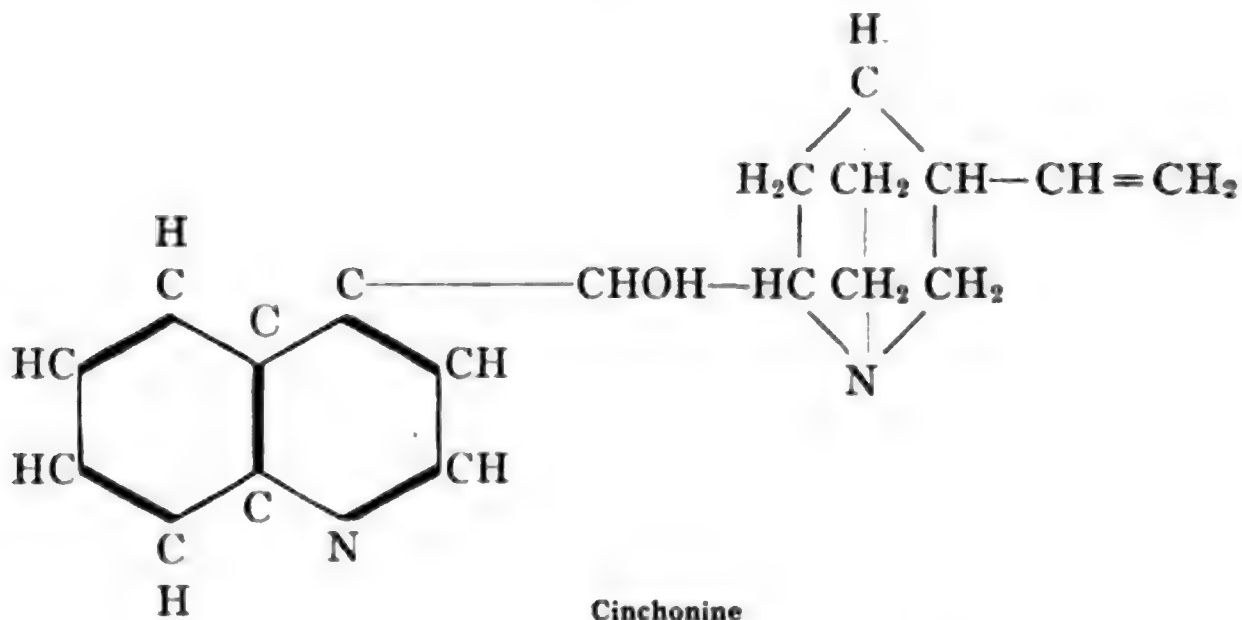
Quinine and Cinchonine

The bark of the cinchona tree, *Cinchona officinalis*, yields several alkaloids. The most important of these cinchona alkaloids is **quinine**, $C_{20}H_{24}O_2N_2$. Associated with it is **cinchonine**, $C_{19}H_{22}ON_2$, and two which are stereo-isomers of these, viz., **quinidine** and **cinchonidine**.

The relation of quinine and cinchonine to quinoline is shown by their oxidation products. As mentioned in connection with quinoline the alkaloid cinchonine when oxidized yields a mono-carboxy quinoline known as **cinchoninic acid**. Similarly quinine yields **quininic acid** which is a meth-oxy derivative of cinchoninic acid.



These reactions indicate that these two alkaloids each contain a quinoline group. In addition to these two derivatives of quinoline, each of the alkaloids yields another acid, which is the same in both cases. It is known as **loiponic acid**. These facts indicate that quinine is a meth-oxy derivative of cinchonine and that each alkaloid consists of two parts, one a quinoline group and the other a complex, $C_{10}H_{16}ON$, or $C_{10}H_{15}(OH)N$. Although neither of the alkaloids has yet been synthesized the probable constitution of the second half has been suggested by **König** and the accepted constitution is as follows:



The other two cinchona alkaloids, **cinchonidine** and **quinidine**, are stereo-isomers of cinchonine and quinine.

The cinchona tree, from the bark of which these alkaloids are obtained, was originally found only on the eastern slope of the Andes in South America. The cultivation of this species, and other species of the same genus, was introduced into Java, India, Ceylon, Jamaica and Australia. At present the production of bark in Java is greater than in any other country. As early as 1639 the cinchona bark was introduced into Europe but it was not until 1792 that an impure alkaloid was isolated and a little later given the name **quina**. In 1820 this impure alkaloid was separated into two compounds named **quinine** and **cinchonine**. The bark contains about 3 per cent quinine combined with acids, **tannic** and **quinic**, from which it is set free by the action of lime. The free base is then extracted with petroleum ether or

chloroform. It is a di-(tertiary nitrogen) base forming salts, sulphates and chlorides, in which form it may be recrystallized and separated from the other alkaloids present. The free base forms a crystalline hydrate melting at 57° , the anhydrous base melting at 173° – 175° . The base is sparingly soluble in hot water but readily in chloroform, alcohol and ether. The natural alkaloid is levo rotatory. The free base forms both acid and neutral salts. The neutral sulphate crystallizes with $7\text{H}_2\text{O}$ and is the common commercial form in which the alkaloid is used. It is sparingly soluble in water.

The physiological action of the cinchona alkaloids is that of an *antipyretic* or *febrifuge*, lowering the body temperature in case of fevers. Quinine retards the action of oxidase enzymes and acts as a poison to certain organisms, especially that of *malaria*. Its first use was as a specific for this form of fever. It has a very bitter taste and in common with other substances of like properties it acts on the alimentary canal causing increased secretion of digestive juices.

Strychnine and Brucine

The two alkaloids **strychnine**, $\text{C}_{21}\text{H}_{22}\text{O}_2\text{N}_2$, and **brucine**, $\text{C}_{23}\text{H}_{26}\text{O}_4\text{N}_2$, occur together in the seeds of nux-vomica, *Strychnos nux-vomica*, found in India, and in the Ignatius bean, *Strychnos Ignatii*, found in the Philippine Islands. The seeds yield from 3–5 per cent of total alkaloids. The alkaloids are extracted from the seeds in practically the same way as quinine from cinchona bark. Both of the free bases are crystalline and slightly soluble in water. They are both mono-acid bases forming soluble sulphates, nitrates and chlorides. **Strychnine** is not colored by sulphuric acid but when moistened with the acid, in the presence of a crystal of potassium bi-chromate, a series of color changes is produced beginning with blue, then violet, red and finally yellow. **Brucine** by similar treatment gives no color changes but with nitric acid gives a red color that changes to violet when a little stannous chloride is added.

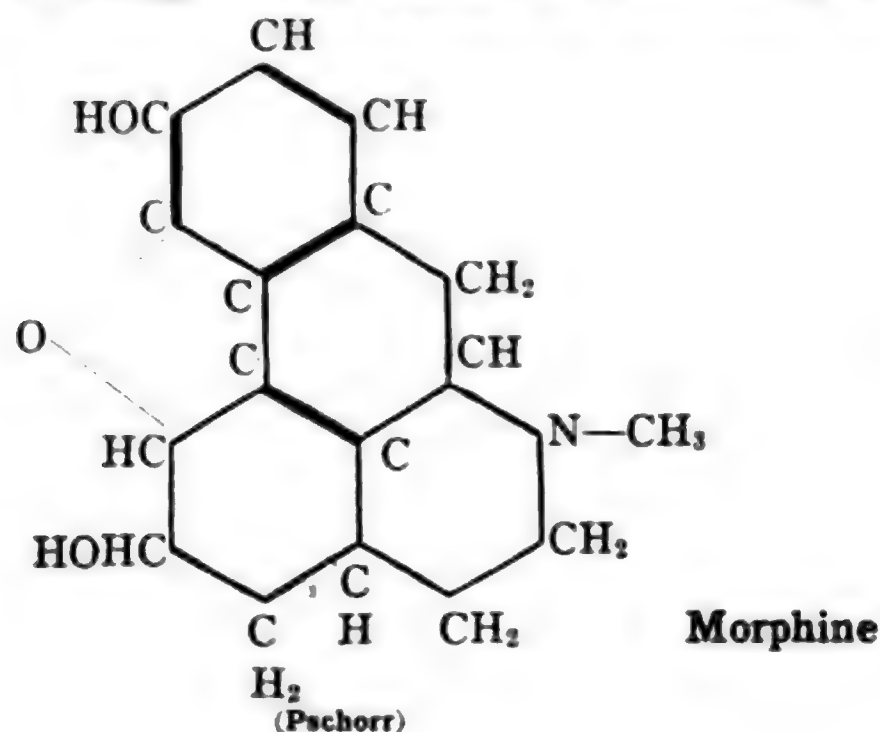
Both of these alkaloids contain a quinoline group but the constitution as developed by a study of their reactions and products of oxidation is more complex than is desirable to discuss here. The relation of the two has been shown to be that brucine is a di-meth-oxy derivative of strychnine which agrees with the composition formulas as given.

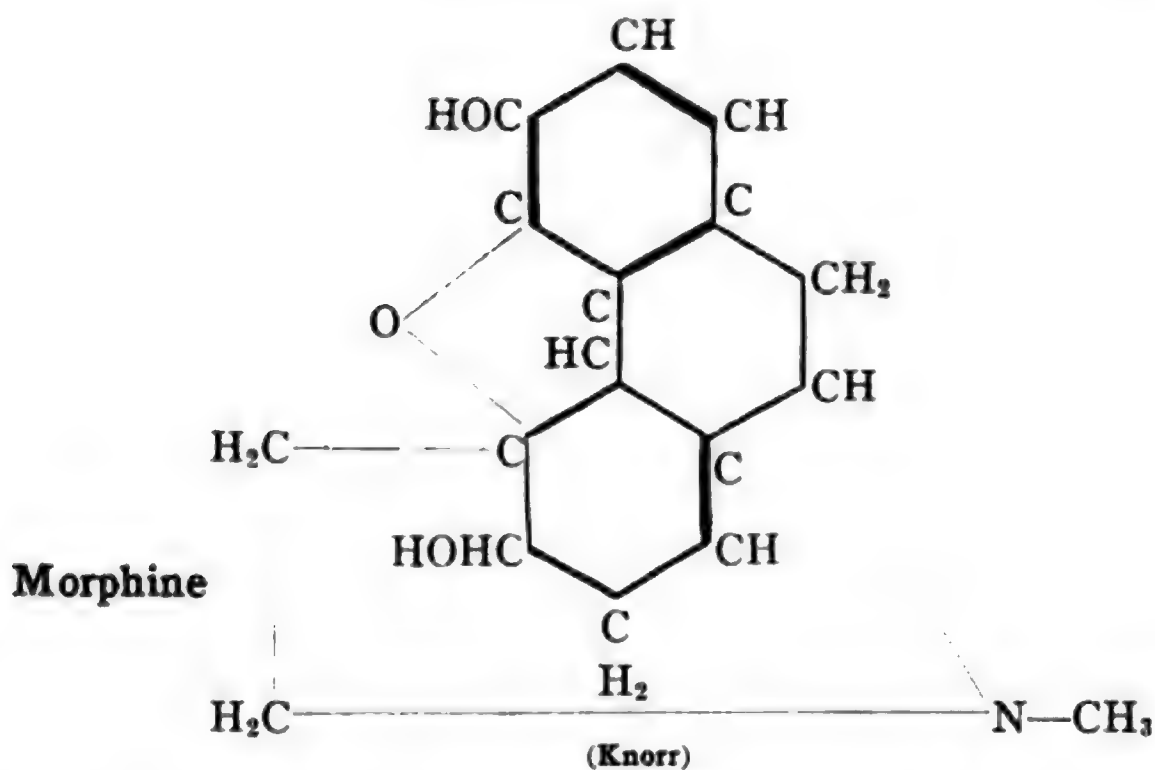
Physiologically the two are similar though brucine is much less

toxic. Strychnine is very poisonous and acts principally on the spinal cord causing convulsions and stopping of respiration. In small doses, as used medicinally, strychnine retards the heart action and increases blood pressure. It is chiefly used as a tonic for local action on the digestive organs and has also been used for chronic alcoholism. The alkaloids are used in the form of their soluble salts or in that of *extract* or *tincture of nux-vomica*.

Morphine, Codeine, Narcotine, Papaverine

The substance known as **opium** yields two very important narcotic alkaloids, viz., **morphine**, $C_{17}H_{19}O_3N$, and **codeine**, $C_{18}H_{21}O_3N$. With these, several other alkaloids are also present, only two of which will be mentioned, viz., **narcotine** and **papaverine**. These opium alkaloids are related not to quinoline but to **iso-quinoline** (p. 865) as is proven by their decomposition products. Codeine has been proven to be the meth-oxy derivative of morphine the two being related as are quinine and cinchonine. Morphine proves to be a di-hydroxyl compound with a third oxygen probably analogous to the oxygen in furfuran. Furthermore, it has been shown that the larger part of the molecule does not contain the nitrogen and is in the form of a **phenanthrene** (p. 807) grouping. All of the evidence indicates that morphine and codeine are derivatives of **3-4-6 tri-hydroxy phenanthrene**. With one of the benzene rings of the phenanthrene nucleus, a pyridine ring is linked, as in isoquinoline. The constitution generally accepted is that suggested by **Pschorr** and modified by **Knorr**.





Cobaine is the methyl-phenyl ether with the hydroxyl hydrogen in position 3 replaced by methyl. Both morphine and codeine are crystalline compounds reacting as tertiary mono-acid bases. Morphine is slightly soluble in water, codeine being more so, the former being more bitter in taste than the latter. The salts are soluble and in this form the alkaloids are used in medicine though codeine is also used as the free base.

Opium.—This well-known substance from which morphine and codeine are obtained is the dried latex (juice) of the unripe fruit of the opium poppy, *Papaver somniferum*. The use of opium as a narcotic has been practised from early times and the poppy plant has been cultivated on a large scale in India, China, Persia and Asia Minor (Smyrna). The opium used in medicine is largely obtained from Smyrna. The recent exclusion of India grown opium from China for opium smoking and the prohibition of its growth in China has greatly affected the production. The number of different alkaloids obtained from opium is very large, larger than from any other one plant. Twenty-five different alkaloids have been isolated, the four principal ones being those mentioned. The percentage amounts of these four in Smyrna opium is as follows:

Morphine	9.00–10.00	per cent
Narcotine	5.00	per cent
Papaverine	0.8	per cent
Codeine	0.3–0.4	per cent

Morphine was first isolated as a pure substance about 1814 and its composition determined in 1831. The isolation of morphine and codeine is similar to that of quinine, by extracting the opium with warm water and then treating the extract with lime. The two are then separated by the different solubility of the free bases.

Physiological Action.—The opium alkaloids are narcotics in their physiological action. Morphine is exceedingly poisonous, the others less so. Their action is on the central nervous system on which they exert both a depressing and exciting influence. Codeine is less depressing than morphine. Morphine is fatal to man in amounts of 0.2–0.3 gram. Continued use of the drug for producing sleep results in tolerance of the body for it and much larger doses are required to produce the usual result.

Heroine.—Two derivatives of morphine, used as synthetic narcotics or hypnotics, deserve attention. The first of these is known as **heroine**. It is the **di-acetyl morphine**. It resembles morphine in its action but does not produce as great mental depression. The second synthetic drug is the ethyl phenyl ether corresponding to codeine. It is known as **dionine**. It resembles codeine in its action. The benzyl phenyl ether is known as **peronine**.

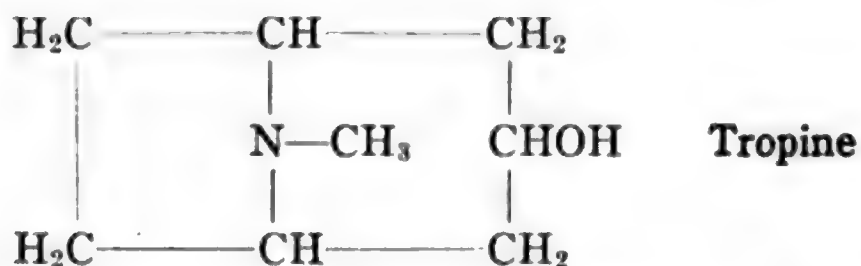
DI-HETERO-CYCLIC ALKALOIDS

Hyoscyamine, Atropine, Tropine

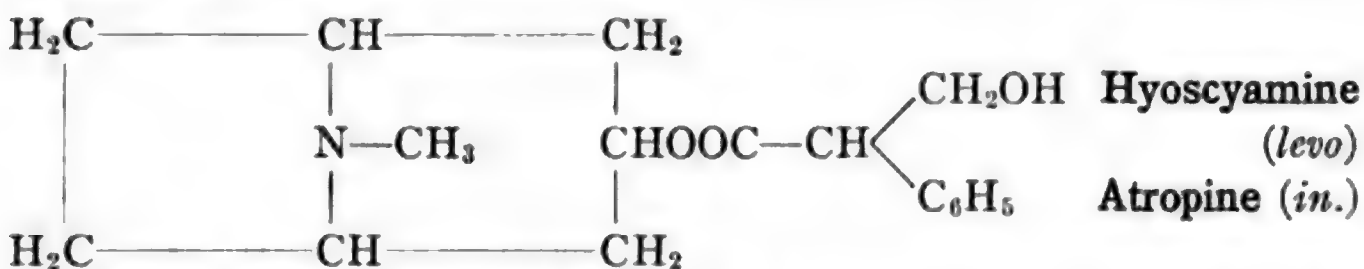
The alkaloids of the next group have the constitution of di-hetero-cyclic compounds. The first three to be considered are **hyoscyamine**, $C_{17}H_{23}O_3N$; **atropine**, $C_{17}H_{23}O_3N$; and **tropine**, $C_8H_{15}ON$. Because of their source they are termed *Solanaceæ alkaloids*, being present in plants belonging to the botanical family of this name. To this same family belong the common edible potato and the poisonous plant known as deadly night-shade, *Atropa belladonna*. Of these three alkaloids hyoscyamine only occurs as a natural alkaloid in the plants. The other two are obtained from it, atropine being a stereo-isomer and tropine a product of hydrolysis. When either **hyoscyamine** or **atropine** is hydrolyzed two products are obtained, one a nitrogen base known as **tropine**, the other an acid, **tropic acid**.



Hyoscyamine and atropine are therefore tropic acid esters of the base tropine. The constitution of tropine according to Willstätter is as follows:



This represents a di-hetero-cyclic compound made up of two conjugated rings with three members common. One of the rings is a *hydrogenated pyridine*, the other a *hydrogenated pyrrole*. As tropine is obtained by hydrolyzing either atropine or hyoscyamine both of these must therefore contain this same grouping. The formula assigned to them is as follows, atropine being the *inactive* variety and hyoscyamine the *levo* form.



Hyoscyamine is found in *Atropa belladonna* (night-shade) and in several species of *Hyoscyamus* from which its name is derived. It is a crystalline compound, m.p. 108.5°, somewhat soluble in water but more readily in chloroform, alcohol or benzene. It is levo rotatory and yields crystalline salts more soluble in water than the base itself. With acids or alkalis hyoscyamine hydrolyzes as previously stated yielding tropine and tropic acid.

Atropine does not occur as such in the solanaceæ plants but is formed from the hyoscyamine present by treatment with dilute alkalis, when isomerization takes place and the inactive form of the alkaloid is obtained. It is crystalline, m.p. 115.5°, and only slightly soluble in water but soluble in alcohol and chloroform. The salts are crystalline and soluble in water.

Tropine is a simpler base than the other alkaloids and is not found as such in the plants but is obtained by hydrolyzing not only atropine and hyoscyamine but other solanaceæ alkaloids as well. It is crystalline, m.p. 63°, and is soluble in water, alcohol, ether or benzene. As shown in its formula it is an alcohol yielding esters with tropic acid,

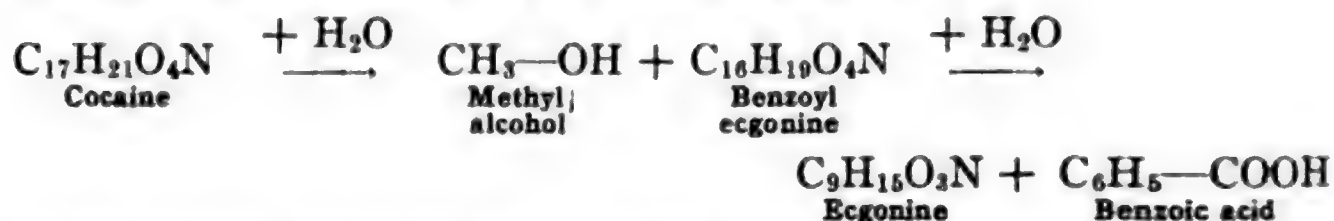
viz., atropine and hyoscyamine. Other esters with organic acids have been prepared and used in medicine.

In their physiological action atropine and hyoscyamine are similar and exert what is termed a *mydriatic* action causing dilation of the pupil of the eye. This action may be produced either by external application or by taking internally. As little as 1 part atropine in 130,000 parts of water will exert a distinct action on the eye. They decrease body secretions and also affect the heart. Taken internally they are poisonous in as little as 0.1 gm. Tropine exerts no mydriatic action when applied to the eye but in large doses internally it does produce dilation. In addition to the use of these alkaloids in the pure form, extracts of belladonna are also used.

Cocaine

Belonging to the same chemical group as atropine is the important alkaloid **cocaine**, $C_{17}H_{21}O_4N$. It is obtained from the leaves of the coca plant, *Erythroxylon coca*, which grows in South America (Bolivia and Peru) and in Java and Ceylon. Distinction should be made between the *coca* plant and the *cacao* bean from which *cocoa* and *chocolate* are made.

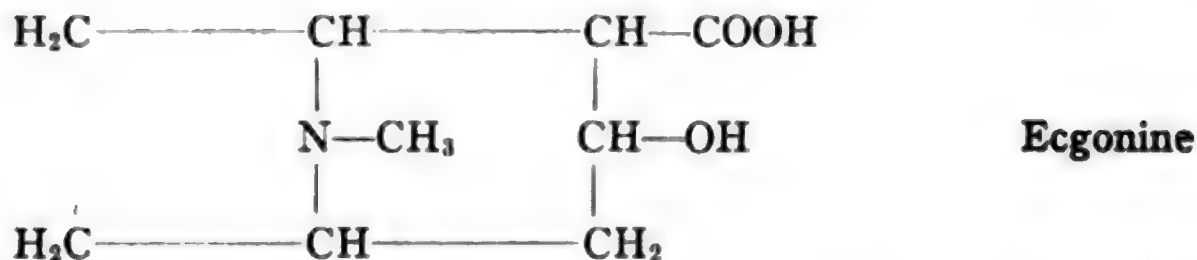
Cocaine like atropine and hyoscyamine hydrolyzes into a simpler nitrogen base and other products. The base is known as **ecgonine** and the other products obtained are **methyl alcohol** and **benzoic acid**. The hydrolysis proceeds in two steps as follows:



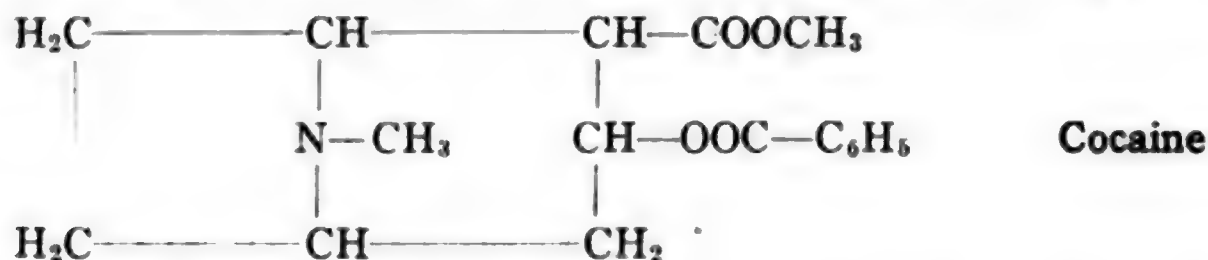
This hydrolysis indicates that the simpler base ecgonine is both an alcohol and an acid and that cocaine is the double ester of this base with benzoic acid and methyl alcohol. **Ecgonine** bears the same relation to **cocaine** that **tropine** does to **atropine**. In its reaction ecgonine proves to be very similar to tropine and as indicated by its composition formula it differs simply by CO_2 .



This indicates that ecgonine is the *mono-carboxyl* derivative of tropine and according to **Willstätter's** formula for tropine ecgonine is as follows:



As cocaine by its hydrolysis proves to be a methyl and benzoyl derivative of ecgonine its constitution is represented by the following formula:



Ecgonine like tropine does not occur as such in plants. The partially hydrolyzed cocaine, viz., the **benzoyl ecgonine**, is a natural plant alkaloid. An ester analogous to cocaine with the radical of **cinnamic acid**, $\text{C}_6\text{H}_5\text{---CH=CH---COOH}$, in place of that of benzoic acid, is a natural alkaloid in Java coca leaves and is known as **cinnamyl cocaine**.

It was known for some time that the natives of Bolivia and Peru chewed coca leaves with lime as a stimulant. The action is due to the alkaloids present in the leaves of which cocaine is the most important. At present both the coca leaves and the crude extract of cocaine are articles of commerce from those countries where the coca plant grows. The alkaloid is extracted with sodium carbonate and petroleum ether. It is a crystalline compound, m.p. 98° , soluble in alcohol, ether, benzene or petroleum ether and slightly soluble in water. It forms well crystallized soluble salts, the hydrochloride being the one mostly used.

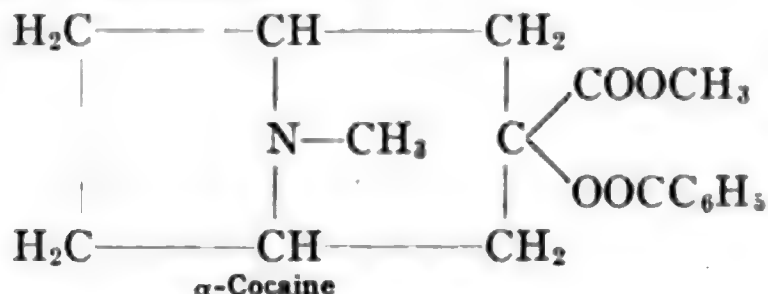
Physiologically, cocaine is an *anesthetic* and a *mydriatic* (dilates the pupil of the eye). It is bitter to the taste and very poisonous. When taken internally it acts on the central nervous system causing paralysis and delusions. The importance of cocaine in medicine is as a local anesthetic, and though used originally for minor operations it is now administered for larger ones. The anesthesia produced is of short duration.

Synthetic Anesthetics

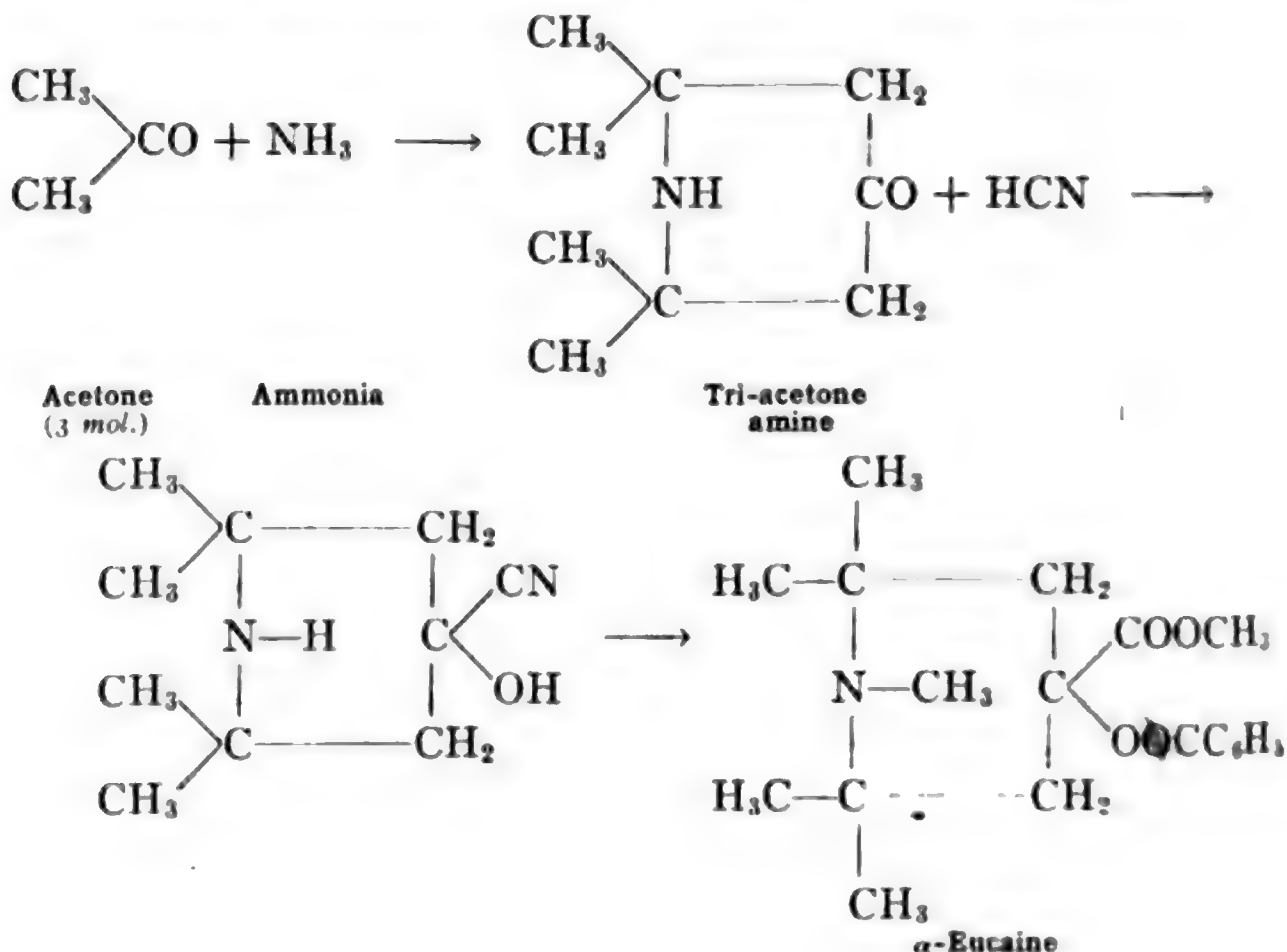
The importance of cocaine in surgery has led to the study of its chemical constitution and to the preparation, by synthetic methods, of analogous compounds having the beneficial anesthetic properties

but free from the highly toxic action of the natural alkaloid. Attention was first directed to the preparation of compounds very similar to cocaine.

alpha-Cocaine.—One of these is isomeric with cocaine and is known as *alpha-cocaine*. In it the carboxyl and hydroxyl are both linked to the same carbon, *i.e.*, the hydroxyl is *alpha* to the carboxyl. Though so similar to cocaine in structure and resembling it in general properties it does not produce anesthesia.

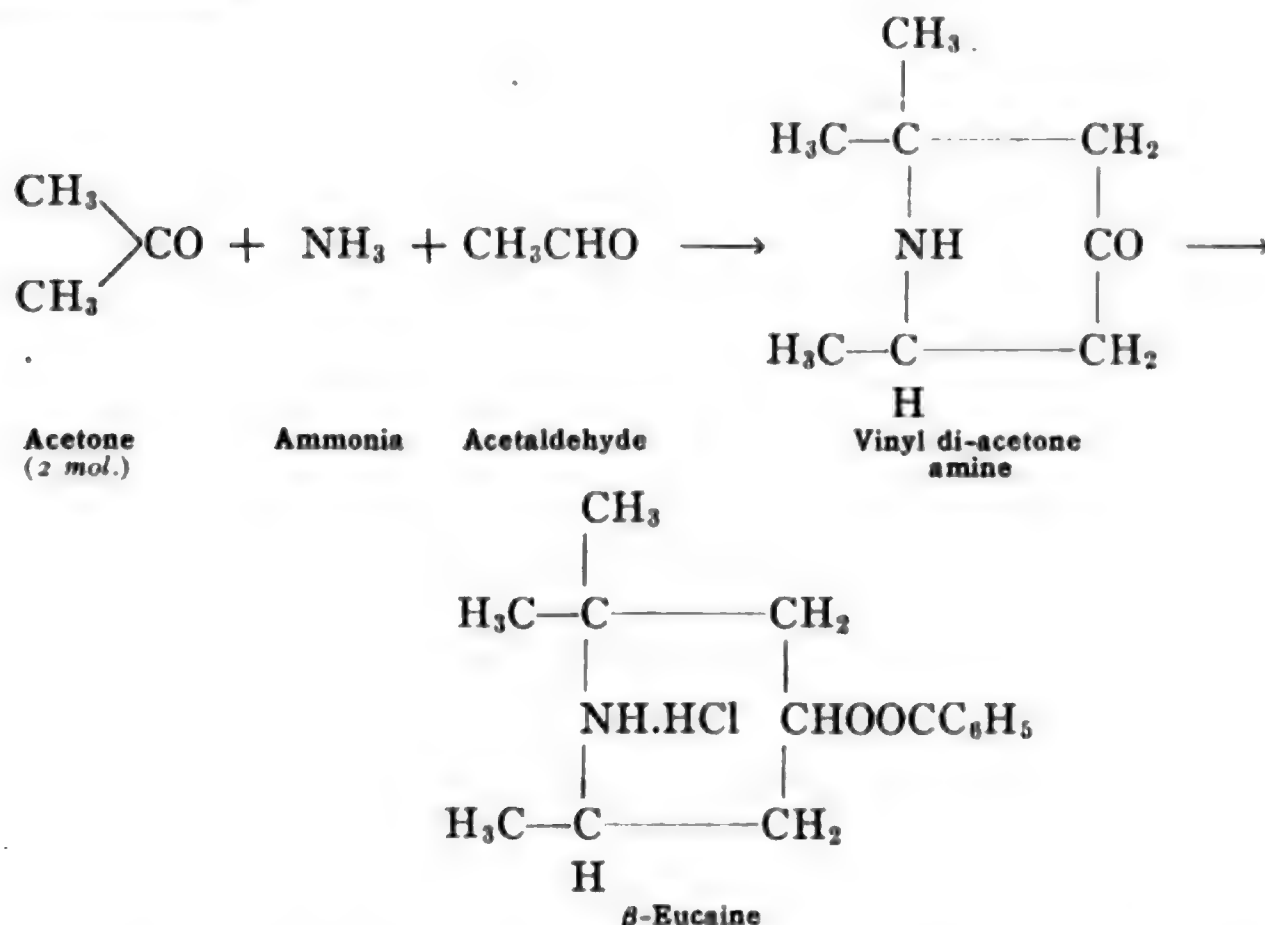


alpha-Eucaine.—A similar compound containing the same pyridine ring as in cocaine and also with the above *alpha-hydroxy* relationship is derived from **tri-acetone amine** and is known as *alpha-eucaine*. Tri-acetone amine by addition of hydrogen cyanide and hydrolysis yields the *alpha-hydroxy acid*. Esterification with benzoic acid and methylation with methyl alcohol then yields *alpha-eucaine*.



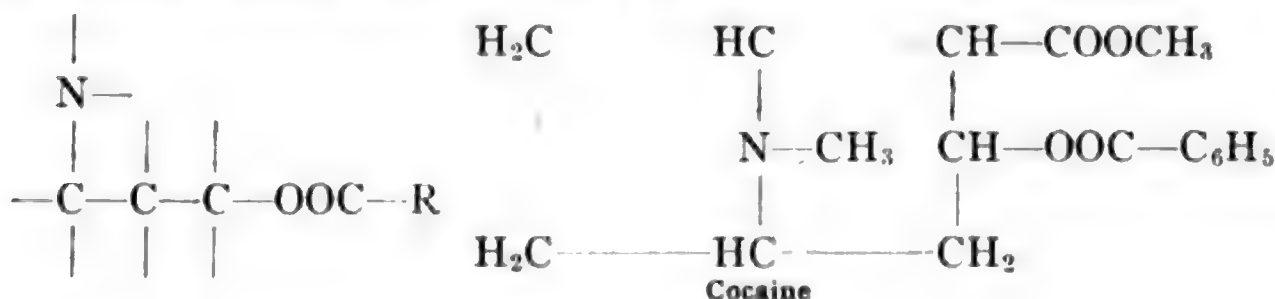
This compound possesses anesthetic properties and is less toxic than cocaine. It is irritating when injected into the body and is now replaced by **beta-eucaine** which is a similar compound derived from **acetaldehyde di-acetone amine, vinyl di-acetone amine**.

beta-Eucaine.—The di-acetone amine yields an alcohol and the benzoyl ester of this, in the form of the hydrochloride salt, is *beta-eucaine*.

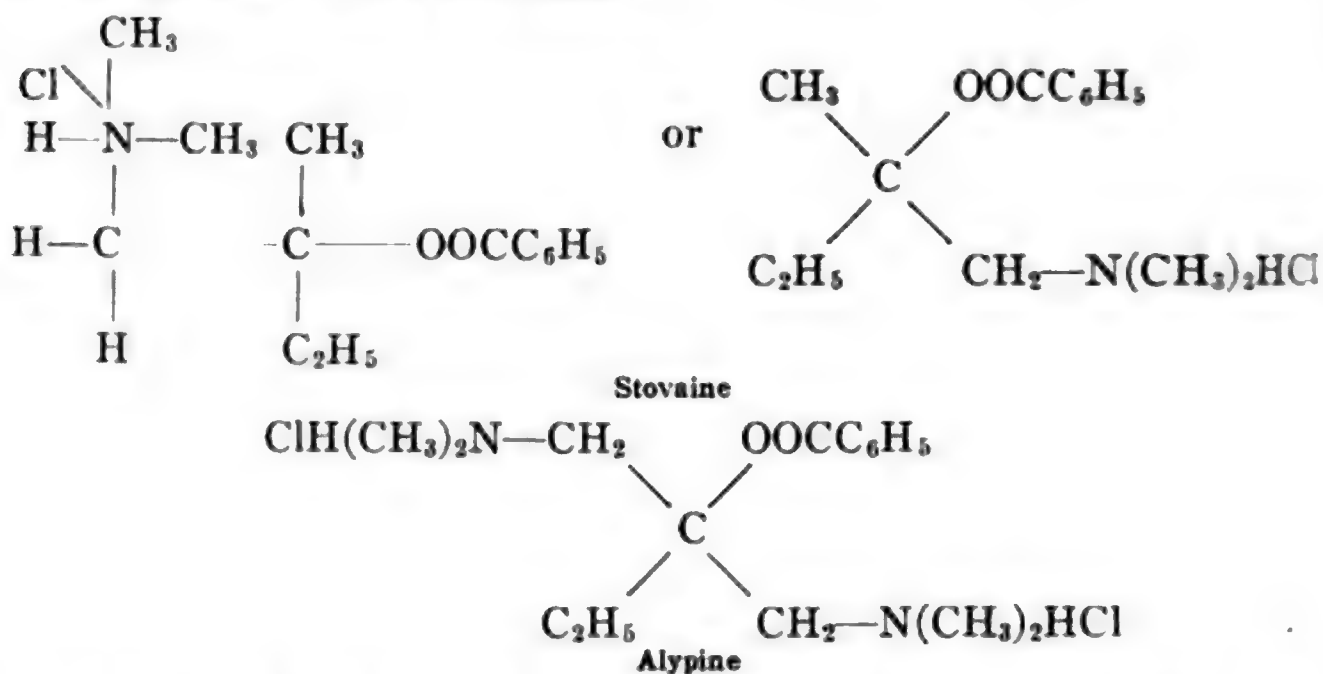


This compound is readily soluble in water, stable at 100° in water solution, is less toxic than cocaine or *alpha*-eucaine and is as strongly anesthetic as cocaine itself.

Stovaine. Aल्पine.—This study of cocaine and eucaine led to the examination of other compounds containing an *alcohol-amine ester* grouping, similar to that present in these anesthetics. The formula for cocaine contains the following grouping:

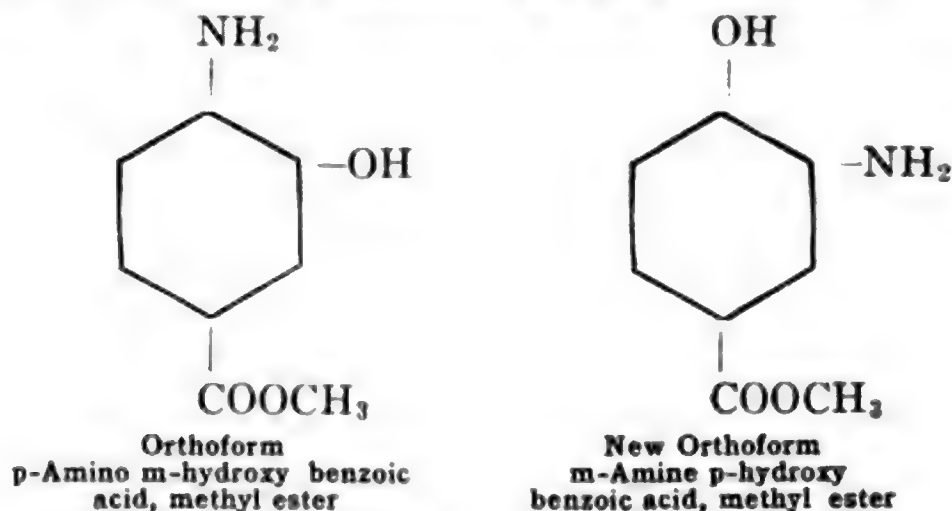


Two important synthetic products containing similar alkamine ester groupings are **stovaine** and **alypine**.



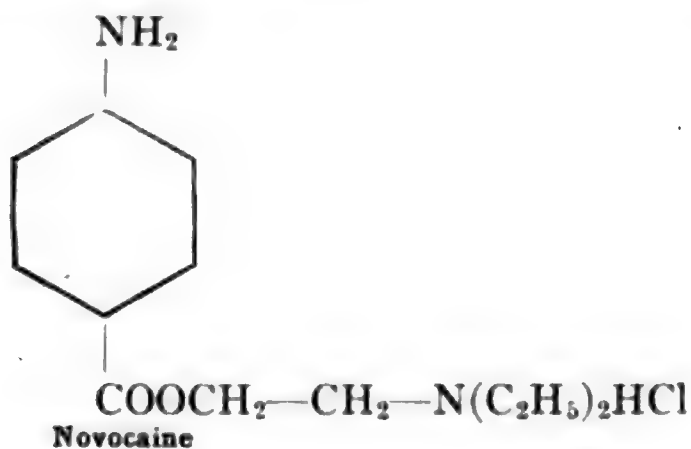
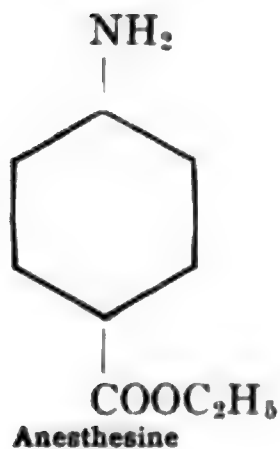
Both stovaine and alypine are very valuable anesthetics being rapid in their action and similar to cocaine without its injurious effects on the heart and respiration. They are used chiefly for spinal anesthesia.

Orthoform.—Another group of synthetic anesthetics are derivatives of **para-amino benzoic acid** or of **amino hydroxy benzoic acids**. Two of these are known as **orthoform** and **new orthoform**.

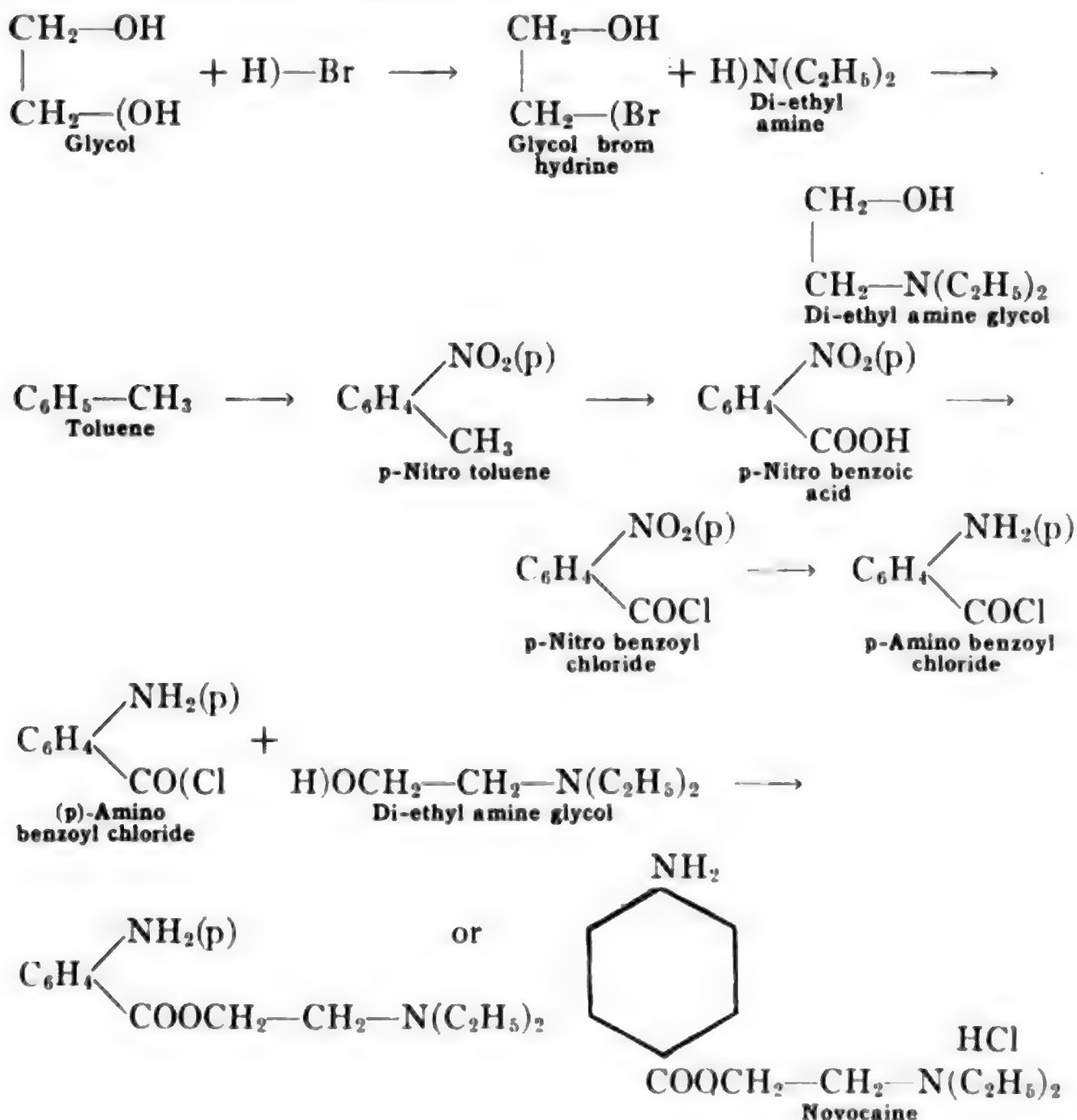


The orthoforms are both anesthetic and antiseptic producing anesthesia when sprayed or dusted upon wounds.

Anesthesine. Novocaine.—Anesthesine, another member of this group, is simply the *ethyl ester* of **para-amino benzoic acid**. A recent very valuable synthetic anesthetic is related to anesthesine and also to cocaine. It is known as **novocaine** and is the *di-ethyl amine* derivative of **anesthesine**.

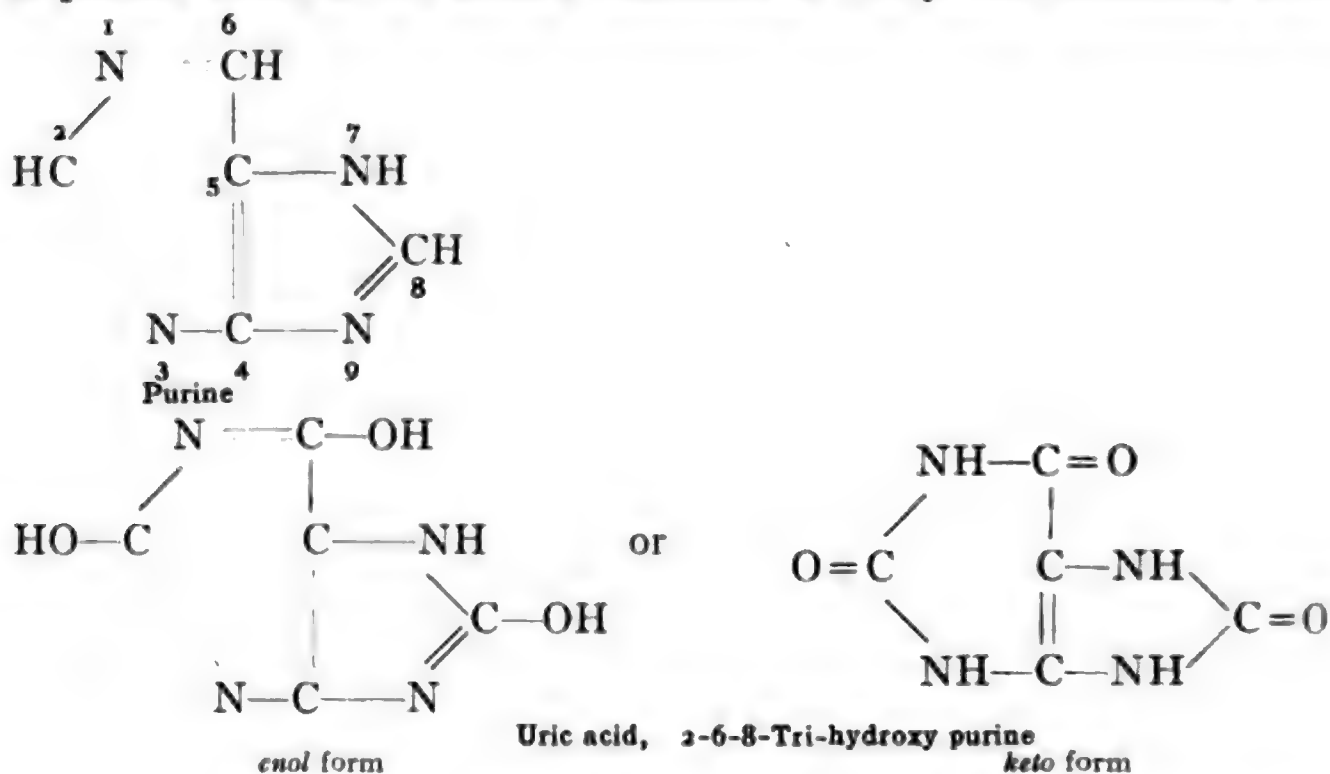


In novocaine it will be seen that there is present the same alkamine ester grouping which is characteristic of cocaine. The compound is prepared by the following reactions.

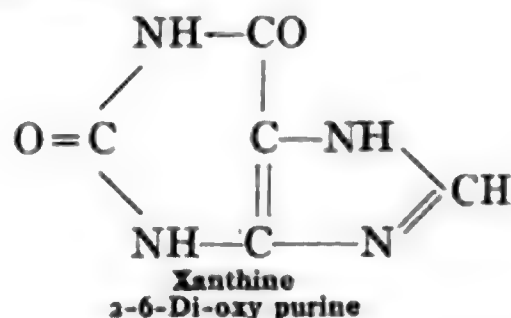
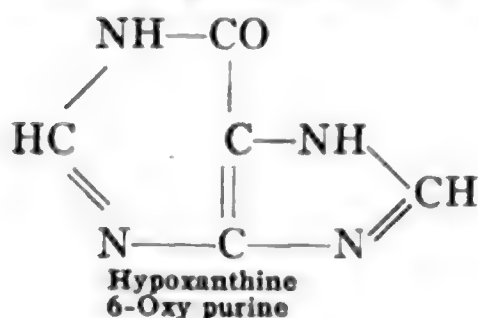


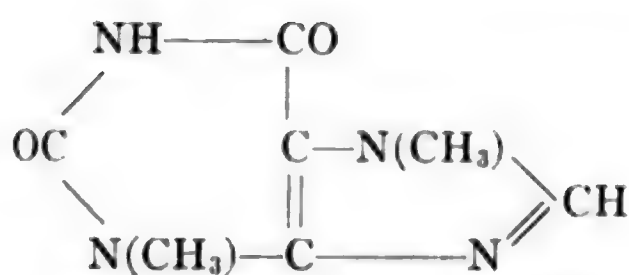
PURINE ALKALOIDS

The purine group of alkaloids includes the vegetable alkaloids **caffeine**, **theobromine**, **theophylline** and the animal alkaloids **xanthine**, **hypoxanthine**, **guanine** and **adenine**. The most common substance which is a purine compound is **uric acid**, but, though directly related to the alkaloids given above, it is not itself usually considered as an alkaloid. The constitution of uric acid has been fully considered (Part I, p. 442). It is the tri-hydroxy derivative of a substance known as **purine** which is the mother substance of the purine alkaloids also.

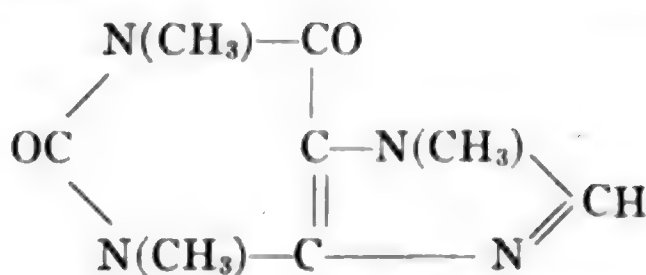


As shown in the above formulas uric acid exists in tautomeric forms, having the constitution either of a *hydroxyl* compound, *enol* form, or of a *ketone*, *keto* form. The purine alkaloids which we have mentioned are similar hydroxyl or amino derivatives of purine. As tautomeric compounds they also exist in the two forms. Those which contain hydroxyl groups have the *enol* and the *keto* forms, while, if they contain ammonia residues instead of hydroxyl, they have the corresponding *amino* or *imino* forms. In the following formulas only one tautomeric form will be given, viz., the *keto* and the *amino*.

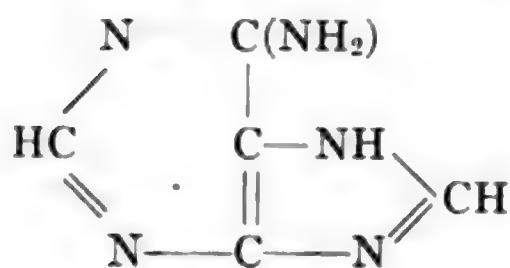




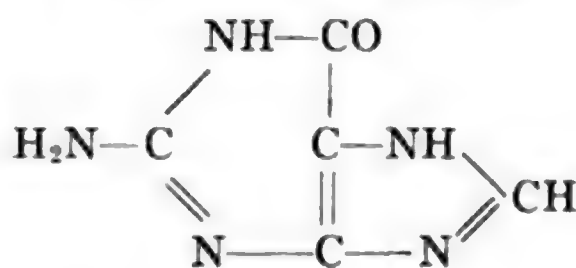
Theobromine and Theophylline (1-3)
3-7-Di-methyl xanthine
or 3-7-Di-methyl 2-6-di-oxy purine



Caffeine
1-3-7-Tri-methyl xanthine
or 1-3-7-Tri-methyl 2-6-di-oxy purine

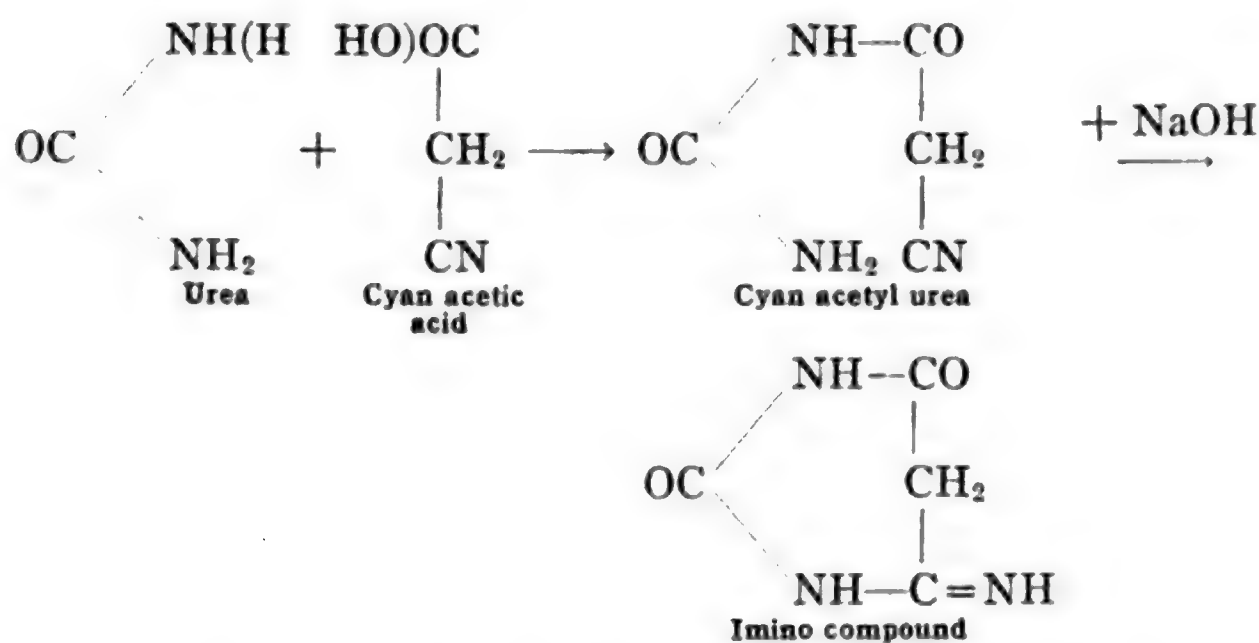


Adenine
6-Amino purine

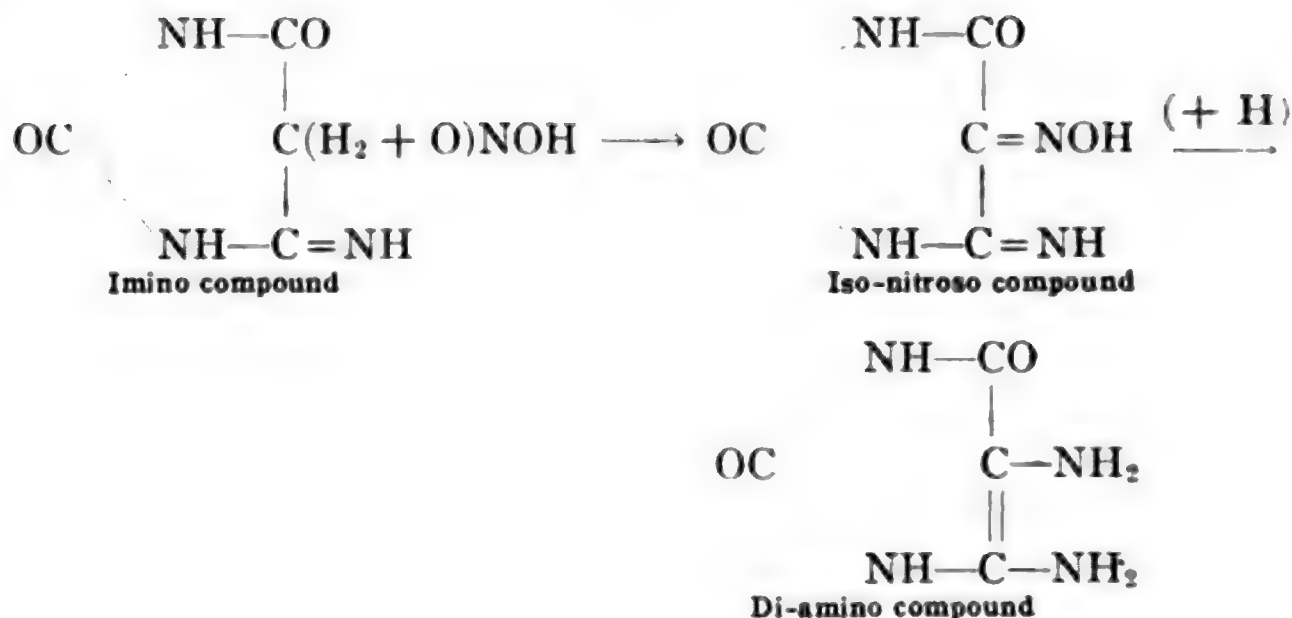


Guanine
2-Amino hypoxanthine
or 2-Amino 6-oxy purine

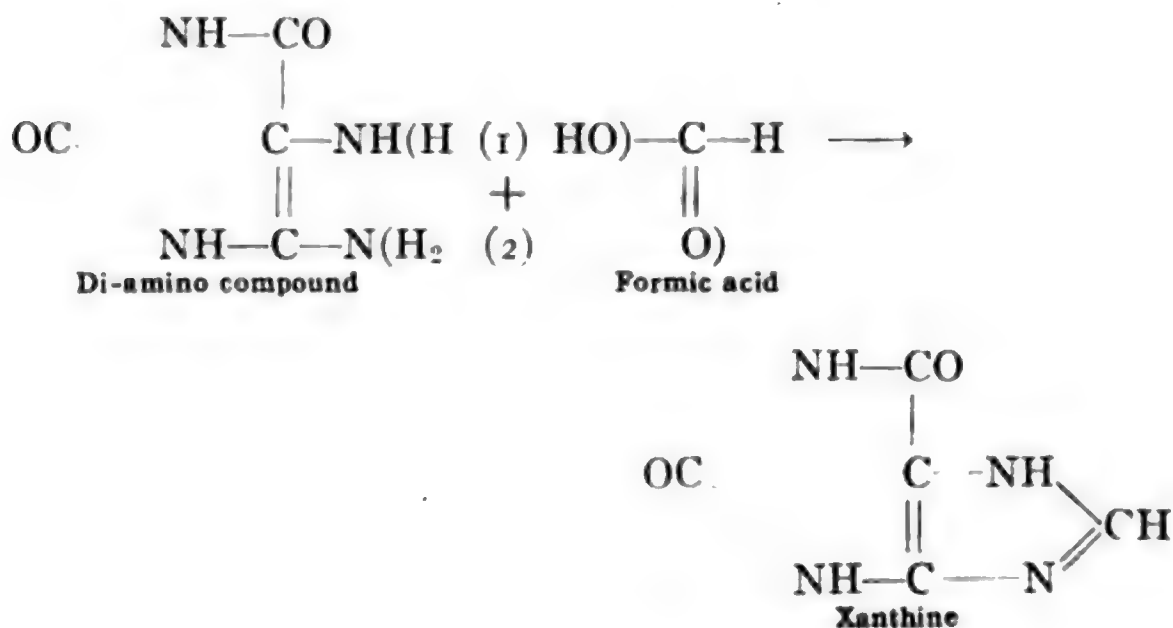
Synthesis of Xanthine.—The synthesis of **xanthine** which is the immediate mother substance of theobromine, theophylline and caffeine has been accomplished as follows: Starting with **urea** or **carbamide**, this is treated with **cyano acetic acid** in the presence of phosphorus oxychloride whereby the cyan acetyl radical is introduced into urea. The cyan acetyl urea by treatment with sodium hydroxide yields an isomeric *imino* compound.



This imino derivative with nitrous acid gives an *iso-nitroso* compound that by reduction with ammonium sulphide yields a *di-amino* compound as follows:



The di-amine is then condensed with **formic acid**, the reaction taking place in two steps as indicated by (1) and (2). The result is **xanthine** which must therefore be **2-6-di-oxy purine**, as follows:



By starting this synthesis with **mono-methyl urea** and introducing another methyl radical into the new amine groups of the di-amine the product is **theobromine**, *i.e.*, **3-7-di-methyl xanthine**. Similarly **di-methyl urea** without further methylation yields **theophylline** which is therefore **1-3-di-methyl xanthine**. **Caffeine** is obtained by starting with **di-methyl urea** and later introducing a third methyl radical in the same position as in theophylline. Caffeine is therefore **1-3-7-tri-methyl xanthine**.

Caffeine, Theobromine, Theophylline

The alkaloid **caffeine** is found in *coffee*, *tea*, and *kola*. It is also known less commonly by the name of **theine**, especially as found in tea. The amount present in coffee and tea is from 1-4.8 per cent in tea and 1-1.5 per cent in coffee. Caffeine crystallizes from water or alcohol, m.p. 234°. It is slightly soluble in water, less so in alcohol and ether and more in chloroform. It acts as a weak base. It may be prepared from either theobromine or from theophylline by further methylation, which confirms the constitution as the **1-3-7-tri-methyl** product.

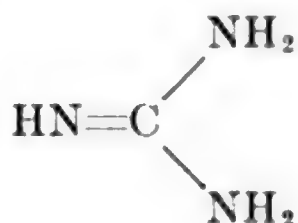
The two alkaloids theobromine and theophylline are isomeric, **theobromine** being the **3-7-di-methyl xanthine** and **theophylline** the **1-3-di-methyl xanthine**. Theobromine is the principal alkaloid of the cocoa bean, *Cacao theobroma*. It occurs also in small amounts in kola nuts and tea leaves. Theophylline is present in small amounts in tea. They both resemble caffeine in being crystalline, weak bases.

Physiologically caffeine, theobromine and theophylline in coffee and tea are mild stimulants, acting on the central nervous system. They seem to increase the capacity of the body for physical exertion, either by acting on the nerves associated with psychical functions, or by increasing the irritability and strength of the muscles. Caffeine also increases blood pressure and respiration. In addition to acting on the nervous system these alkaloids also act on the kidneys, increasing the secretion of urine. This action is regarded as the more important. When taken as food caffeine is excreted in the urine partly unchanged but mostly as **hypoxanthine**, **xanthine** and the *mono-* and *di-methyl* derivatives of the latter.

Xanthine, Hypoxanthine, Adenine, Guanine

These four purine alkaloids are much more important as animal than as plant constituents. Together with **creatine**, **methyl guanidine acetic acid** (p. 441), and **creatinine**, the anhydride of creatine, they constitute the greater part of what are termed the *nitrogenous extractives* of muscular tissue. They are present in ordinary beef extract and may be isolated from it. In addition to being present in muscular tissue they are mostly found in the brain, thymus, liver, kidney, spleen and pancreas. Xanthine and hypoxanthine are also present in *urine*, being the elimination product of **caffeine** in food. Also associated with

them in urine is the non-alkaloid purine compound **uric acid**. Guanine is found most abundantly in *guano* the excrement of sea birds. Adenine and guanine are constituent parts of the complex **nucleic acids** of living cells. Biologically, they all are important products of metabolism. In plants xanthine is found in tea but especially in beet root, lupine seedlings and in yeast. Hypoxanthine is found in barley, potatoes, beet root, black pepper and yeast. It is doubtful if it is present in tea. Adenine is found in yeast, tea and bamboo shoots; guanine in yeast, sugar cane and beet root. The constitution of each of these bases has been fully established as given. Hypoxanthine and xanthine are related as the *mono*- and *di*-oxy derivatives of **purine**. Adenine corresponds to hypoxanthine being **mono-amino purine** while hypoxanthine is **mono-oxy purine**. Guanine is the *mono-amino* derivative of hypoxanthine or **amino oxy purine**. Guanine hydrolyzes and yields both a urea group and a guanidine group, **guanidine** being **imino urea**,



PTOMAINES

Strictly speaking the substances known as ptomaines are not perhaps alkaloids though in many respects they possess the general properties of the group. They do belong to the larger group which includes the alkaloids, viz., that of nitrogen bases. Some of the known representatives are highly toxic while others are very slightly or not at all so and do not show any marked physiological properties. The common knowledge of the substances is in connection with cases of so-called ptomaine poisoning, usually with some form of flesh or milk food which has been kept too long and has begun to decompose. It is at least possible, however, that the poisoning is due, not alone to ptomaines, but rather to toxic substances of bacterial origin. The word ptomaines comes from a Greek word meaning corpse and the substances are so called because they are associated with decomposing flesh. They are not themselves products of bacterial action, *i.e.*, they are not found in the organisms themselves, but they result from the decomposition of pro-

tein material on which molds or bacteria are acting. In higher forms of plant life, such as the fungi, they are stored by the organism, and in green plants they are found in the germ and the roots. In this relationship they are probably nitrogen excretion products of protein metabolism and with them might be included the *amino acids* in general (p. 382), and even all amino compounds. In fact it has been claimed that these simpler nitrogen bases, though many of them are not toxic to human beings, are nevertheless distinctly toxic to plants and therefore have this general alkaloidal property of toxicity.

Considered chemically the ptomaines are in general simpler nitrogen bases than most of the alkaloids and in most cases they are derivatives of *aliphatic amines*.

The exact limits of the group of ptomaines are indefinite but the compounds following are usually included.

Putrescine, Cadaverine

These two compounds have been mentioned previously (p. 193). They are respectively **tetra-methylene di-amine** and **penta-methylene di-amine**.



The relationship of these two compounds to **pyrrolidine** (p. 855) and **piperidine** (p. 857), which they yield by loss of ammonia with the formation of a heterocyclic ring, has been considered. Both of these bases are common putrefaction products of animal bodies as indicated by their names. They both result from bacterial action on *di-amino acids* by *decarboxylation*, i.e., loss of CO₂, and they probably are produced in this way during putrefaction. Besides occurring in decomposed flesh, they have been found also in ergot, in some varieties of cheese, in pathological urine and in putrified soy beans. They are both non-toxic to animals.

Ergot Base, Hordenine

Two bases found in *barley germs* and in *ergot* are closely related compounds. *Ergot* is a fungus growth occurring on cereals, especially rye. From it several alkaloid substances have been isolated. One of these has been shown to be **para-hydroxy phenyl ethyl amine**.



It is to this substance that the principal physiological action of extracts of ergot are due in exerting a strong pressor action on the circulation thus raising the blood pressure. Besides being found in ergot this compound is found also in cheese and in putrid meat.

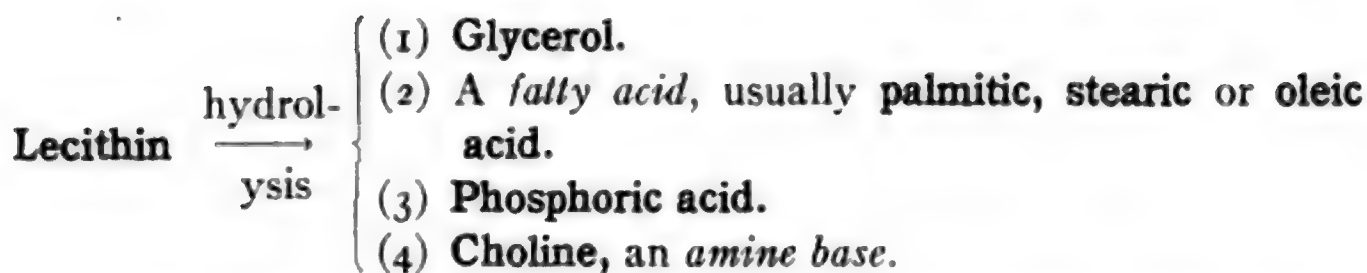
It has been synthesized from **tyrosine, para-hydroxy phenyl alpha-amino propionic acid**, $\text{C}_6\text{H}_4 \begin{array}{c} \text{OH} \\ \diagup \\ \diagdown \\ \text{CH}_2\text{—CH(NH}_2\text{)—COOH} \end{array}$. It is probably derived from this amino acid during the putrefaction of meat.



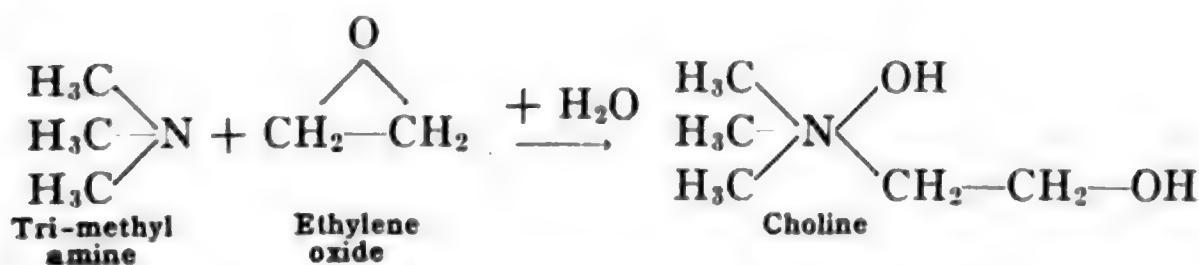
Hordenine is the name of the related base present in the germs of barley, *Hordeum vulgare*. It has been proven to have the constitution of a *di-methyl* derivative of the **ergot base**, as above.

Lecithin, Choline, Neurine

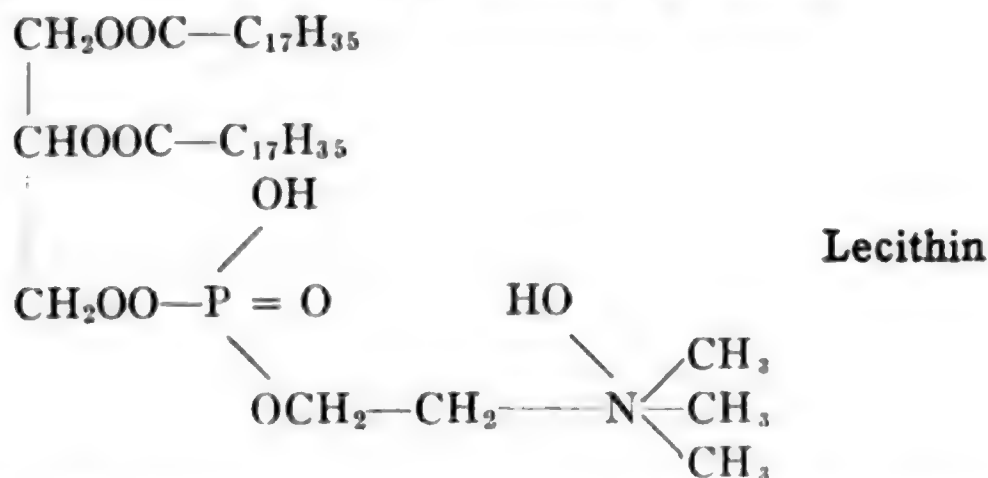
The base **choline** is the mother substance of three other bases, viz., **neurine**, **muscarine** and **betaine**. Choline is very widely distributed having been found in fifty or more animal tissues and plants. The occurrence of most interest is as a constituent part of a substance known as **lecithin**. Although not itself a member of this group of nitrogen bases, lecithin will be considered now in connection with choline. **Lecithin**, or the lecithins, belongs to the group of compounds known as **phospho-lip-ines**. This name signifies the three primary constituents, viz., a *phosphorus*-containing *fat* possessing *basic* or *amino* properties. On complete hydrolysis lecithin yields four products.



Further study has shown that in lecithin the tri-hydroxy alcohol glycerol has *two hydrogens only* replaced by *fatty acid radicals*, while the *third* is similarly replaced by the *phosphoric acid radical*. In case the fatty acid is **stearic acid** the lecithin will be a **glyceryl di-stearate mono-phosphate ester**. Phosphoric acid being *tri-basic*, with only one of its acid groups neutralized by the glycerol, has one of the remaining groups similarly neutralized by the base **choline**. In this base there is present an *hydroxy-ethyl* group which, as an alcohol, is the ester forming group with one of the remaining acid groups of the phosphoric acid. The constitution of choline, which is essential to the complete constitution of lecithin, has been established by several syntheses one of which is from **tri-methyl amine** and **ethylene oxide** in water solution.



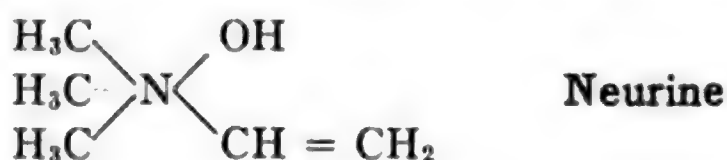
Choline is thus a *quaternary ammonium hydroxide base*, viz., **tri-methyl hydroxy-ethyl ammonium hydroxide**, as in the formula just given. The constitution of lecithin is therefore as follows:



There are different lecithins, due to the particular fatty acid or acids present, the name being that of a group rather than of an individual

compound. Lecithin is a normal constituent of all living cells. Its most common and abundant sources are in egg yolk, fish ova, the brain, nerves and other animal tissues. It is a soft fat-like substance soluble in chloroform, ether, alcohol, benzene and carbon di-sulphide. From alcoholic solution it crystallizes in plates. As choline is a constituent part of lecithin, it is thus found in combination in all those plant and animal tissues where lecithin itself is present. It has been found free in certain seeds and in the cerebro-spinal fluid in disease.

Neurine, the third substance mentioned in this group, is a nitrogen base analogous to choline, being related to it as ethene is related to ethyl alcohol, *i.e.*, neurine is **tri-methyl vinyl ammonium hydroxide**, as follows:

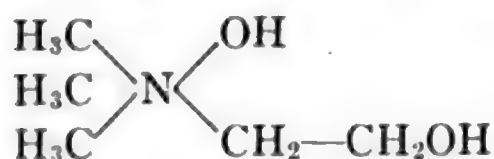


Neurine is a product of the putrefaction of flesh. It has been prepared synthetically from **tri-methyl amine** and **ethylene di-bromide**, and also from **choline**. The constitution as above given is thus thoroughly established.

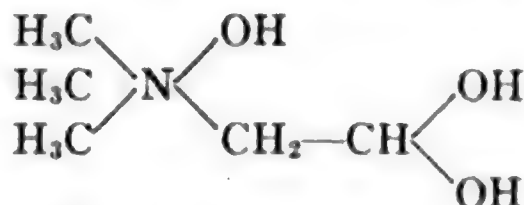
Physiologically choline is primarily a depressant on the circulation but is not strongly toxic. Neurine is similar in its action and 10 to 20 times as toxic as choline.

Muscarine and Betaine

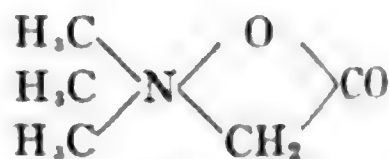
These two bases are related to choline and their constitution has been accepted as that of the corresponding *hydrated aldehyde*, in the case of **muscarine**, and the *acid anhydride* in the case of **betaine**. The formulas of the three compounds show the relationship.



Choline
(alcohol)



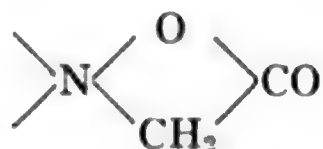
Muscarine
(aldehyde
hydrate)



Betaine
(acid anhydride)

Muscarine is especially interesting in that it is the poisonous constituent of the deadly toad-stool *Aminita muscaria* and of other poisonous fungi. It is a soluble, crystalline, tasteless compound of extreme toxicity.

Betaine derives its name from the fact that it occurs in the molasses obtained from beets, being therefore present in the beet root. It is somewhat widely distributed in plants but not so widely as choline. Betaine is non-toxic and there is even possibility that it may be used as a food material by animals. Like lecithin it is not an individual, but represents rather a group of compounds characterized by the distinctive group



In the foregoing discussion of the alkaloids no attempt has been made to make the study at all exhaustive or complete. Only those individual alkaloids have been considered which are either of general common interest in their properties or use as medicines or that are related pretty directly, in their constitution, to other compounds which we have studied. The chemistry of the alkaloids deals not only with their constitution, which is the main point in the present study, but even more with their biological relationships, both as to their origin and function in plants, and their physiological action upon animals. All of these questions have been very inadequately treated. For further information the student is referred to larger books dealing especially with this most interesting and important group.

Conclusion

With the alkaloids our study of organic chemistry is completed in so far as the purpose of this book requires. Not all compounds or even all groups of compounds have been considered, but with those which have occupied us from the beginning, the student will have as a basis for further study a rather comprehensive knowledge of the most important and outstanding relationships and of individual compounds or groups representing the immense field of organic chemistry, a branch of the science of chemistry which has had a phenomenal development for nearly a century and which is remarkable for its close contact, not only with pure science, but also with industrial and economic problems and with life itself.

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APPENDIX

THE SEPARATION, PURIFICATION, IDENTIFICATION, ANALYSIS AND DETERMINATION OF THE MOLECULAR WEIGHT OF ORGANIC COMPOUNDS

SEPARATION AND PURIFICATION

In the preparation of an organic compound, the product obtained must be separated and purified. If it is a known compound, it may then be identified; while, if it is unknown, it must be analyzed and its molecular weight determined.

Separation of Liquids.—The methods of separation are of two general types, one for liquids and the other for solids. A liquid product may consist of the entire reaction mixture, or it may be obtained as a distillate. The product may contain acid or alkali or it may be mixed with water, alcohol or other liquids used in the reaction or obtained as secondary products.

If the mixed liquid product does not separate into two distinct layers of non-miscible liquids, such separation is sometimes brought about by the addition of water. The two liquids are then separated by means of a separatory funnel and the one containing the desired product is washed with water to free it from any acid or alkali present. The washing is accomplished by adding about an equal volume of water, shaking thoroughly and then separating a second time. The washing and separating may need to be repeated several times. If the crude separated product is known to be strongly acid, or to contain substances, *e.g.*, bromine, easily removed by alkali, then a little alkali is added with the first wash water. Similarly, if the crude product is known to be strongly alkaline, a little acid may be used in the first wash water. When the product is thoroughly washed, the water, still held as a physical mixture, is removed by the addition of a dehydrating agent, such as *concentrated sulphuric acid*, *anhydrous calcium chloride*, *anhydrous potassium carbonate* or *solid potassium hydroxide*. In some cases, the drying may be accomplished by placing the product in a desiccator. After standing over the dehydrating agent until the

watery, opaque liquid is clear, it is separated by decantation and the practically pure, dry product is then distilled.

If the product finally obtained is an individual compound it will distil at approximately a constant temperature which is the boiling-point of the compound. If the product is a mixture of two compounds that can be separated by fractional distillation, this method is then used as in the case of the separation of alcohol and water, which is a common laboratory exercise illustrating this process. It usually results that compounds so separated are only partially pure, each being mixed with a little of the other. In some cases, two compounds can not be separated in this way, because their boiling-points are too close together. By conversion into derivatives, *e.g.*, esters, the boiling-points of which lie farther apart, fractional distillation may be made possible. The conditions of distillation may also vary as some compounds must be distilled under diminished pressure.

Separation of Solids.—The separation of solid compounds involves the process of crystallization. The solid compound, obtained as the result of a reaction, may be insoluble in the reaction mixture or it may be soluble. In case it is insoluble it is filtered off and washed, the style of filtration differing according to the nature of the product. A crystalline residue is usually filtered on a Buchner funnel with the aid of suction but, if the residue is fine and packs, it is better to filter through an ordinary filter paper or through a fluted paper. The washed residue is then dissolved in an appropriate solvent and crystallized. Sometimes the insoluble residue consists of the desired compound mixed with other insoluble compounds. In this case the residue is extracted with an appropriate solvent and the compound crystallized from the solution.

If the desired compound is soluble in the reaction liquid, the solution is separated from any insoluble residue by filtration, usually through a fluted filter paper. The solution containing the compound is then ready for crystallization.

Crystallization.—To crystallize a soluble compound out of its solution, the solution is evaporated, not too rapidly, to incipient crystallization, the hot solution filtered and the clear filtrate allowed to cool. By slow cooling from incipient crystallization large crystals are usually obtained, while evaporation of the solution beyond incipient crystallization, followed by rapid cooling, usually yields a more abundant product of purer and finer crystals. After cooling, the crystalline

product is filtered on a Buchner funnel, with suction, the crystals washed slightly with fresh solvent and, if necessary, recrystallized one or more times in order to secure a pure product. The ease of solubility of the compound in the solvent used affects the procedure. If a compound is much more soluble in hot solvent than in cold, the mere cooling of the hot solution may yield abundant product and the greater part of it. If, however, the compound is almost as soluble in cold solvent as in hot, the solution must be evaporated in order to bring about crystallization.

After a crystalline product of sufficient purity has been obtained the crystals must be dried to remove external moisture or other solvent. This is accomplished either by warming, by allowing the crystals to stand in a desiccator, by pressing them between folds of filter paper, by placing them on a porous unglazed plate, or by simply exposing them to warm dry air. The amount of heat allowable in drying a crystalline compound depends upon its melting point and upon the presence or absence of water of crystallization.

After pure dry crystals have been obtained they are then ready for identification, analysis or preservation.

IDENTIFICATION

The identification of an organic compound, in case it is of known composition, constitution and properties, involves simply the determination of its physical constants. The physical constants, the determination of which is usually sufficient for the purpose, are the *melting-point*, the *boiling-point* and the *specific gravity*.

Determination of Melting-Point.—The determination of the melting point of a solid compound, usually obtained in a crystalline form, is accomplished by introducing a very little of the finely powdered substance into a fine, thin-walled capillary tube, known as a melting-point tube. This tube is then fixed in close contact with the bulb of a thermometer and the two immersed, to the depth of about one-half inch above the thermometer bulb, in sulphuric acid or some other liquid, which is then gradually heated to the known or supposed melting-point. The temperature reading of the thermometer, at the instant the compound within the capillary melts, is the *melting-point*. The heating is often accomplished in a small round-bottom flask which is clamped

by the neck so that it may be warmed by the small flame of a burner held in the hand and moved around slowly. A better form of apparatus is the special melting-point bulb devised so as to secure slow, uniform heating of the thermometer and the compound in the affixed melting-point capillary tube.

If the compound melts sharply, within a range of a degree or two and within a degree or two of the theoretical melting-point, it is usually sufficient proof of identity. Repeated determinations should be made to insure good results.

In the case of some compounds with low melting-point and of fats and oils, which are not individual compounds, the temperature at which the liquid substance solidifies is determined rather than the melting-point. This is termed the *solidification-point* or *freezing-point*.

Determination of Boiling-Point.—It is not usual to determine both the melting-point and the boiling-point of the same compound, for one of the two often comes outside of the range of ordinary laboratory operations. The melting-point is generally determined in the case of compounds that are solid at ordinary temperatures, and the boiling-point in the case of those that are liquid.

The boiling-point of a liquid compound is determined by simply distilling a little of the pure dry compound using a small distilling flask with a thermometer carefully placed in the neck of the flask so that the top of the mercury bulb is just below the outlet. Wrapping the neck of the flask and the thermometer with asbestos paper, to prevent sudden cooling by drafts of air, is a precaution that insures more accurate results.

Determinations so made are subject to corrections for the thermometer and for the fact that part of the thermometer column is outside of the vapor of the boiling liquid. Boiling-points described as "*corrected*" have had the above corrections made. As the boiling-point of a liquid varies with the pressure it is also necessary to designate the barometric pressure under which the determination is made.

Determination of Specific Gravity.—The determination of the specific gravity, usually in the case of liquids only, is made by means of a pycnometer or specific gravity bottle. The pycnometer is filled with the liquid, at a definite temperature, and weighed. The weight of the pycnometer empty, and the weight of it when filled with water at a definite temperature, must also be known or must be determined.

From the data thus obtained the specific gravity may be calculated from the equation:

$$\text{Sp. Gr.} = \frac{\text{Wt. Vol. of Liquid}}{\text{Wt. equal Vol. of Water}}$$

The temperature at which the water is weighed should be 4° , the temperature of its maximum density, but it may be some other. The temperature at which the liquid is weighed may be 4° also, or it may be any arbitrary temperature, *e.g.*, 15° , which is a commonly accepted standard. These temperatures should always be given as part of the recorded constant and are expressed as follows: Sp. Gr. $\frac{15^{\circ}}{4^{\circ}}$ means that the temperature of the liquid was 15° and that of the water was 4° . Sp. Gr. $\frac{15^{\circ}}{15^{\circ}}$ or $\frac{4^{\circ}}{4^{\circ}}$ means that the temperature of the two liquids was the same and as indicated.

ANALYSIS

In organic compounds, the elements ordinarily determined by what is termed *ultimate analysis* are *carbon, hydrogen, oxygen, nitrogen, sulphur* and one of the *halogens*. Other elements may sometimes be present but we shall not consider their determination here.

Qualitative Tests.—To test an organic compound qualitatively is a simple matter. The presence of *carbon* which, of course, is found in all organic compounds, is proven by heating some of the compound with copper oxide, or in an atmosphere of oxygen gas. *Carbon dioxide* is thereby formed and is identified by absorption in lime water with the production of a precipitate of calcium carbonate. A still simpler method is to heat the compound slowly on a piece of platinum foil. Charring and then burning proves the presence of carbon; no ash being left, unless the compound is a metal salt or an organo-metallic compound.

The same method as the first one given above is used for the detection of *hydrogen*, its presence being proven by the formation of *water* as the result of oxidation.

Nitrogen is tested for by either of two methods. A little of the dry compound is mixed with an equal amount of dry *soda-lime* and heated in a small tube until charring and then complete decomposition takes place. The formation of *ammonia gas*, detected by means of a piece of

red litmus paper held in the mouth of the tube, proves the presence of nitrogen. The other method is known as the *cyanide test*. When an organic nitrogen compound is fused with metallic *sodium*, *sodium cyanide* is formed. By heating the acidified solution of the fused mass with a ferrous iron salt, *sodium ferro cyanide* is produced and the presence of this is shown by the formation of a blue precipitate of Prussian blue on the addition of a little *ferric chloride* solution.

Sulphur, in the *unoxidized* condition, is tested for by heating the compound with *metallic sodium* or with *sodium carbonate*, by which treatment the sulphur is converted into *sodium sulphide*. If the fused product is placed on a silver coin and moistened, a spot of *silver sulphide* will be produced. The fused mass may also be dissolved in water, neutralized with nitric acid, and a little lead acetate solution added. The formation of a black precipitate of *lead sulphide* proves the presence of sulphur. These tests are applicable only in case the sulphur is in an *unoxidized* form. To test for sulphur in either the *oxidized* or *unoxidized* form a little of the compound is boiled with strong *nitric acid* or is heated with *sodium peroxide*. This treatment converts the sulphur into the form of *sulphuric acid* or a *sulphate*, either of which will yield a white precipitate of *barium sulphate* when tested with barium nitrate in the presence of nitric acid.

The halogens, *chlorine*, *bromine*, and *iodine*, are tested for by heating the compound with *lime*, free of halides, acidifying the solution of the fused mass with nitric acid and testing with silver nitrate. A precipitate of *silver halide* proves the presence of a halogen.

In the study of organic compounds resulting from organic laboratory preparations, it is seldom necessary to carry out a complete qualitative analysis as the elements present are generally known.

Quantitative Determination.—The quantitative determination, of the amount of each element present in an organic compound, is ordinarily termed *organic combustion* as combustion or oxidation takes place in all of the determinations.

Carbon and Hydrogen by Combustion.—When an organic compound is heated in the presence of *copper oxide* or in a stream of pure *oxygen gas*, it is oxidized or burned. If the oxidation is complete, all of the carbon of the compound is converted into *carbon dioxide* and all of the hydrogen into *water*. The combustion is carried out in a long tube of hard glass, or of fused quartz, known as a *combustion tube*.

The tube is heated in either a gas or an electric combustion furnace. Details as to filling the tube and heating will not be given here as they pertain more properly to text books of analytical chemistry. The products of oxidation pass from the combustion tube through apparatus for the absorption of gases; first for the absorption of water and then of the carbon dioxide. The absorption of water takes place in tubes containing properly prepared, non-basic *anhydrous calcium chloride* or pure concentrated *sulphuric acid*. The increase in the weight of the tube during the combustion gives us the amount of *water* produced, and from this the amount of *hydrogen* may be calculated. The absorption of carbon dioxide takes place in *potash bulbs* (**Liebig** bulbs or some modification of them) which contain a solution of *potassium* or *sodium hydroxide*, of proper concentration. The increase in the weight of these bulbs gives the amount of *carbon dioxide* produced, from which the amount of *carbon* may be calculated.

Nitrogen by the Dumas Method.—Two methods are used for the determination of *nitrogen*, viz., the **Dumas** method and the **Kjeldahl** method. The Dumas method is also known as the *absolute method* and is a dry combustion operation similar to the one for carbon and hydrogen. When an organic compound containing *nitrogen* is heated, in the presence of *copper oxide* or pure *oxygen gas*, the nitrogen is converted into some of its oxides. Before leaving the heated combustion tube the products of oxidation are passed over coils of pure *reduced copper*. The oxides of nitrogen are reduced by the copper and free nitrogen gas is the final product. The nitrogen gas is collected in a special gas burette which contains a solution of potassium or sodium hydroxide to absorb carbon dioxide. After the combustion is completed the pure nitrogen gas is transferred from the burette to a eudiometer tube, measured under atmospheric conditions, the volume reduced to standard conditions of temperature and pressure (0° and 760 mm.), and, from the final *volume of pure nitrogen gas*, the *weight of nitrogen* is calculated.

Nitrogen by the Kjeldahl Method.—The absolute method, while the more accurate and often used when the results of analysis are for the purpose of determining the empirical formula of a compound, is sometimes replaced by the **Kjeldahl** or wet combustion process. In outline the method is as follows: The organic compound is decomposed and oxidized by heating for some time in about 30 cc. of pure con-

centrated sulphuric acid. A catalyzer and other reagents for special purposes are sometimes added. The result, however, so far as the nitrogen is concerned, is the conversion of all of the *nitrogen* of the organic compound into *ammonia* which, in the presence of the sulphuric acid, is held as *ammonium sulphate*. After the completion of the acid digestion or oxidation the liquid is cooled, diluted with water and a strong solution of *sodium hydroxide*, more than sufficient to neutralize the sulphuric acid, is added. The flask containing the liquid is then quickly connected with a condenser and the free ammonia is distilled into a *standard solution* of hydrochloric or sulphuric acid. After the distillation has been continued long enough to drive over all of the ammonia, the standard acid, which has absorbed the liberated ammonia, is titrated back with a corresponding *standard alkali*. This gives us the amount of standard acid in excess, and by subtracting this from the amount of standard acid originally used, we obtain the amount of standard acid neutralized by the liberated ammonia and from this the amount of *ammonia* produced. From the amount of ammonia produced we may calculate the amount of *nitrogen* in the original compound or we may calculate the amount of nitrogen directly from the amount of standard acid neutralized. The Kjeldahl method has great advantages as to the time required for a determination, and is accurate enough for many organic nitrogen determinations.

Sulphur by the Carius Method.—*Sulphur* in organic compounds is commonly determined by either the **Carius** method or the **Liebig** method. The Carius method consists in heating a small amount of the compound in a sealed tube with pure *fuming nitric acid*. By this treatment the sulphur is converted into *sulphuric acid*, which is then determined in the usual way by precipitation as barium sulphate. The tubes in which the heating is carried out are known as *Carius tubes* and are of hard glass, one end only being sealed at the beginning. As long as the tube is open, the compound and the nitric acid are kept separate, one being introduced into the tube itself and the other into a small tube or vial which can be slipped into the larger tube. After the materials have been placed in the tube the open end is sealed by fusion, the tip being drawn out to a thick walled capillary. Care must be taken not to mix the contents until the tube is sealed and cooled. When cold, the tube is tipped so that the compound and acid become thoroughly mixed. The tube is then placed in a heavy iron oven.

known as a *bomb oven*, and heated to a temperature of about 200° – 250° for some hours. The temperature and the length of time of heating vary somewhat with the compound. After cooling, the tube is carefully opened, by heating the capillary tip, and then, with the aid of a file, the tube is broken in two near the capillary end. The contents are carefully washed out into a beaker and the determination of sulphur in the form of *sulphuric acid* is then completed by the customary procedure, proper precautions being observed as to details.

Sulphur by the Liebig Method.—By the **Liebig** method the compound is fused, with sodium or potassium hydroxide, in a silver crucible. When fused, a little potassium nitrate is added as an oxidizing agent. The sulphur of the organic compound is thus converted into *sodium* or *potassium sulphate*. The fused mass is dissolved in water, acidified with nitric acid, and the sulphur precipitated as *barium sulphate* by the addition of *barium nitrate*.

Halogens by the Carius Method.—The halogens, *chlorine*, *bromine*, *iodine*, are also determined by the **Carius** method. In this case, crystalline *silver nitrate*, *nitric acid* and *the compound* under examination are all introduced into the Carius tube. The nitric acid must be kept separate from the compound until after the tube is sealed. After sealing the tube as before, the contents are mixed and the tube heated in the bomb oven. The halogen of the organic compound is converted into *silver halide* which, when the tube is opened, is carefully washed out, filtered, and weighed.

Oxygen by Difference.—The only element, usually present, which has not been directly determined is *oxygen*. If the determinations made do not total to approximately 100 per cent and if no other element is present, the difference between 100 *per cent* and the *sum of the determinations* made is the *per cent of oxygen* in the compound.

EXAMPLE OF THE CALCULATION OF THE PERCENTAGE COMPOSITION AND THE EMPIRICAL FORMULA, FROM THE DATA OF ANALYSIS

A compound *dry* and with *no water of crystallization* yielded the following results:

Carbon and Hydrogen by Combustion

Wt. compound taken.....	0.5645 g.
Wt. CO ₂ obtained.....	0.8415 g.
Wt. H ₂ O obtained.....	0.4314 g.
Carbon: C in CO ₂ = 27.27 per cent; $0.2727 \times 0.8415 \text{ g.} =$	0.2295 g.
0.2295 g. carbon in 0.5645 g. compound =	40.65 per cent
Hydrogen: H in H ₂ O = 11.11 per cent; $0.1111 \times 0.4314 \text{ g.} =$	0.0479 g.
0.0479 g. hydrogen in 0.5645 g. compound =	8.48 per cent

Nitrogen by the Kjeldahl Method

Wt. compound taken.....	0.5215 g.
$\frac{N}{2}$ HCl in absorption flask.....	20.0 cc.
$\frac{N}{10}$ NaOH for back titration.....	12.0 cc.
$\frac{N}{10}$ HCl equivalent to 20.0 cc. $\frac{N}{2}$ HCl.....	100.0 cc.
$\frac{N}{10}$ HCl neutralized by NH_3 = 100.0 cc. - 12.0 cc. =	88.0 cc.
$\frac{N}{10}$ HCl; 1.0 cc. is equivalent to NH_3 , 0.0017 g. or <i>nitrogen</i> =	0.0014 g.
<i>Nitrogen</i> = 88.0 \times 0.0014 g. =	0.1232 g.
0.1232 g. <i>nitrogen</i> in 0.5215 g. compound =	23.62 <i>per cent</i>

Empirical Formula.—The calculation of the *empirical formula* from the *percentage composition* is as follows:

Element	Per cent	Atomic weight	Relative proportions, in atoms	Relative number of atoms	Empirical formula
C	= 40.65 \div	12	= 3.4 \div 1.7	= 2	C_2
H	= 8.48 \div	1	= 8.5 \div 1.7	= 5	H_5
N	= 23.62 \div	14	= 1.7 \div 1.7	= 1	N
O	= 27.25 \div	16	= 1.7 \div 1.7	= 1	O
(by difference)					

The percentage amount of each element is divided by the atomic weight of the element. This gives the relative proportions of each element in atoms. These numbers are not, however, whole numbers but, by dividing each by the smallest one found, we obtain whole numbers which represent the relative number of atoms in the compound. The formula of the above compound is thus found to be C_2H_5ON or some multiple of it. Such a formula is known as an *empirical formula*. It agrees with the percentage composition of the compound, but it may or may not be the true molecular formula. Any multiple of it would likewise agree with the percentage composition. The only way that we can decide on the true molecular formula is by knowing the molecular weight of the compound, as the formula C_2H_5ON corresponds to a molecular weight of 59; the formula $C_4H_{10}O_2N_2$, to a molecular weight of 118 and the formula $C_6H_{15}O_3N_3$, to a molecular weight of 177.

DETERMINATION OF THE MOLECULAR WEIGHT OF AN ORGANIC COMPOUND

The molecular weight of an organic compound is usually ascertained by one of three determinations, viz.,

(a) The *vapor density* of the compound,

(b) The *rise in the boiling-point* of a solution of the compound above that of the pure solvent.

(c) The *lowering of the freezing-point* of a solution of the compound below that of the pure solvent.

Vapor Density by the Victor Meyer Method.—The *vapor density* of a compound is the *relative weight of a volume of it, in the gaseous condition, compared with the weight of an equal volume of hydrogen*. If this vapor density is known, it is possible to calculate the weight of a *gram-molecular volume* and thus the *molecular weight*. The method of procedure most frequently used is that known as the **Victor Meyer** method, which, in fact, while not actually weighing a definite volume of the gas determines the *volume of air displaced by a definite weight of the compound* after it is converted into the gaseous condition. The apparatus consists of a long tube with an enlarged lower end and with a bent side arm through which the displaced air may be driven out into a eudiometer tube. The compound is weighed into a small stoppered or sealed vial, introduced into the tube and then vaporized by heat. The heating is accomplished by placing the above described tube in a larger glass tube or outer jacket containing some liquid, often water, which, when boiled, raises the temperature of the inner tube above the boiling-point of the compound under examination. The heat of the outer boiling liquid and its vapor expands the liquid compound in the vial, forces it open and volatilizes the compound. The compound thus converted into the gaseous condition drives out of the upper part of the inner tube a *volume of air equal to the volume of gas produced*. The expelled air is collected in a eudiometer tube and accurately measured. The method is limited to those substances, usually more or less volatile liquids, which boil at temperatures below the boiling-point of water or some other liquid that is applicable. After the operation is completed, the eudiometer tube is carefully transferred to a tall cylinder of water and the volume of air contained in it is read at *atmospheric temperature and pressure*. The volume of air in cubic

centimeters must then be corrected to *standard conditions of temperature and pressure* (0° and 760 mm.). We thus have a volume of air equal to the volume of gas resulting from the volatilization of a known weight of compound. In other words, we have the *weight of a definite volume of a compound in the gaseous condition* and from this we calculate either the weight of a liter or the weight of a *gram-molecular volume*, viz., 22.4 liters. This gives us as a final result the *molecular weight*.

EXAMPLE OF THE CALCULATION OF THE MOLECULAR WEIGHT OF A COMPOUND FROM
THE DATA OF A VAPOR DENSITY DETERMINATION

A compound of the empirical formula CH_2O and with a boiling-point of 105° gives the following data as the result of a determination of the vapor density by the Victor Meyer method.

Wt. Compound taken.....	0.240 g.
Volume of air in eudiometer at 18° and 750 mm.....	96.4 cc.
Volume of air reduced to 0° and 760 mm. (see below).....	87.3 cc.
87.3 cc. = volume of gas from.....	0.240 g.
1000.0 cc. gas =	2.748 g.
22400.0 cc. (22.4 liters) =	61.5 g.
Molecular weight =	61.5

A compound of the formula CH_2O corresponds to a molecular weight 31.

A compound of the formula $\text{C}_2\text{H}_4\text{O}_2$ corresponds to a molecular weight 62. Therefore the molecular formula of the compound determined is $\text{C}_2\text{H}_4\text{O}_2$.

The reduction of a volume of a gas represented by " V ," measured at temperature " t " and pressure " P ," to the volume at standard conditions, viz., 0° and 760 mm., is accomplished by the application of the physical equation:

$$V_0 = \frac{PV}{760(1 + \alpha t)}$$

As the air was measured over water, the pressure, as read on the barometer, must be corrected for the tension of water vapor " w " at the temperature " t ." This makes the equation:

$$V_0 = \frac{(P - w)V}{760(1 + \alpha t)}$$

Substituting the value of " w " at 18° which is 15.33 mm. and the value for " P " = 750 mm.; " V " = 96.4 cc., and " α " = 0.00366, we have

$$V_0 = \frac{(750 - 15.33)96.4}{760(1 + 0.00366 \times 18)}$$

$$V_0 = 87.3 \text{ cc.} = \text{volume of air at } 0^{\circ} \text{ and 760 mm.}$$

Rise in Boiling-Point and Lowering of Freezing-Point.—The other two determinations, which enable us to calculate the molecular weight, are based on the fact, that when a non-ionized substance is dissolved in a solvent, the boiling-point of the solution will be raised above that of the pure solvent, and the freezing-point of the solution will be lowered below that of the pure solvent, by a certain amount, depending upon the *weight of the solvent*, the *weight of the substance* and upon its *molecular weight*. Stated in another way, and more specifically: a *gram-molecular weight of any non-ionized compound when dissolved in 1000 grams of the solvent will raise the boiling-point, or lower the freezing-point, of the solvent a constant amount*. These constants are termed the *molecular rise of boiling-point* or the *boiling-point constant* and the *molecular lowering of the freezing-point* or the *freezing-point constant*. The values of these constants for solvents commonly used are:

BOILING-POINT CONSTANTS

Solvent	Gram-molecular weight of any non-ionized compound dissolved in	
	1000 g. solvent	100 g. solvent
Water.....	.52°	5.2°
Alcohol.....	1.15°	11.5°
Acetone.....	1.67°	16.7°
Ether.....	2.11°	21.1°
Acetic acid.....	2.53°	25.3°
Ethyl acetate.....	2.61°	26.1°
Benzene.....	2.67°	26.7°
Phenol.....	3.04°	30.4°
Chloroform.....	3.66°	36.6°

FREEZING-POINT CONSTANTS

Solvent	Gram-molecular weight of any non-ionized compound dissolved in	
	1000 g. solvent	100 g. solvent
Water.....	1.86°	18.6°
Acetic acid.....	3.90°	39.0°
Benzene.....	5.00°	50.0°

The problem, therefore, is to have apparatus enabling us to determine accurately the rise in the boiling-point and the lowering of the freezing-point when a known weight of a compound is dissolved in a known weight of the solvent. From this we can calculate the weight of compound necessary to produce the molecular rise or lowering and this amount will be the molecular weight of the compound. The pieces of apparatus used in these determinations and the procedure in carrying out a determination are complicated, and a description in more detail in this book seems out of place. Great care must be observed in carrying out a determination and various corrections must be applied. The result obtained, so far as its application to organic chemistry is concerned, is that we obtain, in the end, the molecular weight of the compound in question and this is essential in order to use the data of analysis for the purpose of determining the molecular formula of a compound.

EXAMPLE OF THE CALCULATION OF THE MOLECULAR WEIGHT OF A COMPOUND FROM
THE DATA OF DETERMINATIONS OF RISE IN BOILING-POINT AND
LOWERING OF FREEZING-POINT

The compound used in the example of the analysis for carbon, hydrogen, nitrogen and oxygen, and which gave results from which the empirical formula was calculated to be C_2H_6ON , gave the following results for the rise in boiling-point of ether.

Wt. compound taken.....	0.350 g.
Wt. solvent (ether).....	52.850 g.
Rise in boiling point observed.....	0.25°

The physical equation for calculating the molecular weight from the rise in boiling-point is as follows:

$$M = C \frac{100 w}{R W}$$

- In this equation
- “ M ” = the *molecular weight*
 - “ C ” = the *boiling-point constant* for 100 g. solvent
 - “ w ” = the *weight of compound* in grams
 - “ W ” = the *weight of solvent* in grams
 - “ R ” = the *rise of boiling-point* in degrees.

From our data, then, we have as follows:

$$M = 21.1 \frac{100 \times 0.350}{0.25 \times 52.85}$$

$$M = 55.87$$

The molecular weight of 55.87 corresponds more nearly to the molecular formula C_4H_5ON , with calculated molecular weight of 59, than to the formula $C_4H_{10}O_2N_2$ or $C_6H_{15}O_3N_3$ with calculated molecular weights of 118 and 177. Very close agreement between the calculated and determined values is not usual in practice, nor is it necessary, as it is only required to select between molecular weights that are quite different in value.

The same compound was used for the determination of the lowering of the freezing-point of water. The data obtained are as follows:

Wt. substance,	0.525 g.
Wt. solvent (water),	55.320 g.
Lowering of freezing-point,	0.30°

The physical equation for deriving the molecular weight from the freezing-point lowering is analogous to the one which applies to the rise in boiling-point. It is as follows:

$$M = C \frac{100 w}{L W}$$

" L " = observed *lowering of freezing-point*

" C " = *freezing-point constant* for 100 g. solvent.

Substituting in this equation the values obtained in the determination we have:

$$M = 18.6 \frac{100 \times 0.525}{0.3 \times 55.32}$$

$$M = 58.8$$

The molecular weight is therefore 58.8, according to the determination, and the formula of the compound must be C_2H_5ON with the theoretical molecular weight of 59.

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